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GLYCEMIA IN CACHEXIA OF NURSLINGS

E. JASO, M.D.
Assistant Physician, Provincial Institute of Puericulture
MADRID, SPAIN

Cobliner [1] found that the blood sugar was lower in malnourished infants than in normal ones. He obtained amounts as low as 0.5 mg. of dextrose per thousand cubic centimeters of blood. He made the interesting observation that as soon as the conditions of nutrition improved the blood sugar was increased.

Brown [2] discovered that the average dextrose content of the blood was 0.77 mg. per thousand cubic centimeters in hypothreptic infants whose weights were 50 per cent lower than normal. If the weight was from 50 to 80 per cent of normal, the blood sugar reached an average of 0.91. From this observation he inferred that glycemia and the degree of denutrition maintain a certain relationship.

Tisdall, Drake and Brown [3] observed that the average dextrose content of the blood in atrophic infants was 0.76 mg. per thousand cubic centimeters.

Wilson, Levine and Gottschall [4] stated that the blood sugar in athreptic infants, when fasting, was 0.59 mg. per thousand cubic centimeters. Vitetti [5] did not find that the blood sugar in thirteen hypothreptic infants, when fasting, differed from that of normal babies, the average being 0.78.

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From the service of Dr. Bravo and Dr. Muñoyerro, Provincial Institute of Puericulture.

1. Cobliner: Blutsuckeruntersuchungen bei Säuglingen, Ztschr. f. Kinderh. **1**:207, 1911.

2. Brown, M. J.: Quart. J. Med. **18**:175, 1925.

3. Tisdall, F. F.; Drake, T. G. H., and Brown, A.: The Carbohydrate Metabolism of Marantic Infants, Am. J. Dis. Child. **30**:829 (Dec.) 1925.

4. Wilson, J. R.; Levine, S. Z., and Gottschall, G.: IX. The Respiratory Exchange in Marasmus: Carbohydrate Metabolism of Normal and Marasmic Infants With and Without the Administration of Insulin, Am. J. Dis. Child. **36**: 470 (Sept.) 1928.

5. Vitetti, G.: Contributo sperimentale al comportamento della curva glicemica in bambini iponutriti sottoposti alla cura insulinica, Pediatria **36**:1210, 1928.

According to the data presented by Macciotta,[6] the average blood sugar in four atrophic patients was 0.71 mg.; on recovery, this average was increased to 0.84.

Nervi [7] in a recent work gave the amount of blood sugar both in atrophic and dystrophic children as between 0.58 and 0.82 mg. per thousand cubic centimeters, the average being 0.72.

From an analysis of these figures the conclusion is drawn that the degree of glycemia in dystrophic infants is lower than in normal ones. The figures given by the authors mentioned show an average blood sugar of 0.72 mg. in dystrophic infants. Considering 0.88 as the normal average for nurslings, this average is seen to be 18.9 per cent lower.

EXPERIMENTAL DATA

We have determined the blood sugar in fifty-four infants with various chronic disturbances who were hypothreptic or athreptic, at the Provincial Institute of Puericulture. We employed the Bang II method [8] according to the technic used in the Laboratory of General Pathology of Dr. Novoa Santos by Dr. Outeirino. We made all the determinations in infants who had had no nourishment for at least three hours (from three to four as an average). The heel was the spot selected for the taking of blood. In some cases, however, because of the serious condition of the child, it was impossible to obtain blood from this source; in these cases we resorted to puncture of the longitudinal sinus, which we did with a syringe that was carefully washed, passed through distilled water and wiped scrupulously.

Other technical details followed by us were as follows: All tests that required more than one minute for the blood-taking maneuvers and weighing of the paper containing the blood were set aside, as it is a well known fact, confirmed by experience, that speed is necessary to insure accuracy. We made three tests for every determination, computing the average amount from the figures obtained separately, and rejecting a test if its results deviated from those of the other two. The table gives the figures obtained by us.

The average of all blood sugar values found in merely nutritional (not infectious) cachexia, i. e., in the first forty observations, is 0.53 mg. per thousand cubic centimeters.

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6. Macciotta, G.: Sulla somministrazione di glucosio per via sottocutanea nella gravi intossicazione di origine alimentare e nella atrofie dei lattanti, Pediatria **37**:283, 1929.

7. Nervi, C.: La glicemia e le curve glicemiche alimentari nell'infanzia, Pediatria **38**:251, 1930.

8. Durupt: Microméthodes et semi-microméthodes appliquées aux analyses chimiques du sang et des humerus, Paris, A. Poinat, 1924, p. 78.

Blood Sugar of Fifty-Four Infants with Various Chronic Disturbances

Number	Age, Months	Weight, Gm.	Disturbances in Nutrition	Feeding	Blood Sugar, Mg. per 1,000 Cc.	Observations
1	4½	3,550	Athrepsia	Milk and cereals	0.73	
2	2	2,640	Athrepsia	Breast	0.44	Habitual vomiting
3	3	2,450	Athrepsia	Mixed	0.59	
4	2½	2,450	Hypothrepsia, 2d grade	Mixed	0.78	
5	2½	2,950	Athrepsia	Mixed	0.59	
6	2	3,050	Hypothrepsia, 2d grade	Mixed	0.65	Habitual vomiting
7	1	2,640	Hypothrepsia, 2d grade	Breast	0.82	Hypo-alimentation
8	3	2,850	Athrepsia	Mixed	0.56	
9	4	3,320	Hypothrepsia, 2d grade	Mixed	0.79	
10	7	3,440	Athrepsia	Artificial	0.30	Agonic. B. of the sinus
11	2	2,375	Athrepsia	Mixed	0.375	Agonic. B. of the sinus
12	6	3,790	Athrepsia	Artificial	0.475	Habitual vomiting
13	2	2,540	Athrepsia	Mixed	0.48	Blood from the sinus
14	4	3,230	Hypothrepsia, 2d grade	Mixed	0.435	Habitual vomiting
15	2	2,540	Athrepsia	Mixed	0.115	Agonic. B. of the sinus
16	1½	2,750	Hypothrepsia, 2d grade	Breast	0.47	Habitual vomiting
17	2	2,440	Athrepsia	Breast	0.325	Habitual vomiting
18	2	2,250	Athrepsia	Breast	0.12	Blood from the sinus
19	1½	2,645	Hypothrepsia, 2d grade	Maternal breast	0.40	
20	6	5,045	Hypothrepsia, 2d grade	Breast and cereals	0.585	
21	1	2,640	Hypothrepsia, 2d grade	Mixed	0.68	
22	1	3,185	Hypothrepsia, 2d grade	Breast	0.69	
23	3	2,265	Athrepsia	Breast	0.30	Infant weak
24	12	4,265	Hypothrepsia, 2d grade	Cereals	0.74	
25	3½	3,950	Hypothrepsia, 2d grade	Breast and cereals	0.73	
26	4½	3,500	Athrepsia	Breast and cereals	0.103	
27	3½	2,950	Hypothrepsia, 2d grade	Breast and cereals	0.77	
28	4½	3,715	Hypothrepsia, 2d grade	Mixed	0.43	
29	2	2,570	Hypothrepsia, 2d grade	Breast	0.37	
30	2	3,245	Hypothrepsia, 2d grade	Breast	0.665	Convalescing from toxicosis
31	4	.....	Athrepsia	Mixed	0.40	
32	2	3,180	Hypothrepsia, 2d grade	Mixed	0.575	Convalescing from toxicosis
33	7½	4,300	Hypothrepsia, 2d grade	.....	0.44	
34	2	2,910	Hypothrepsia, 2d grade	Breast	0.525	Habitual vomiting
35	4½	2,930	Athrepsia	Mixed	0.38	
36	6	3,350	Hypothrepsia, 2d grade	.....	0.45	
37	2	2,780	Athrepsia	Breast	0.39	
38	5	2,950	Hypothrepsia, 2d grade	Breast and cereals	0.635	Infant weak
39	5½	3,350	Hypothrepsia, 2d grade	Breast and cereals	0.605	
40	15½	4,960	Hypothrepsia, 2d grade	Cereals	0.875	
41	5	2,850	Athrepsia	Breast	1.02	Congenital syphilis
42	1	3,200	Hypothrepsia, 2d grade	Mixed	0.875	Congenital syphilis
43	11	4,700	Hypothrepsia, 2d grade	Mixed	0.885	Congenital syphilis
44	1½	2,670	Hypothrepsia, 2d grade	Mixed	0.77	Congenital syphilis
45	2	2,440	Athrepsia	Mixed	0.44	Congenital syphilis
46	7	3,520	Athrepsia	Mixed	1.02	Tuberculosis
47	3	3,050	Athrepsia	Breast	0.895	Tuberculosis
48	6	3,765	Hypothrepsia, 2d grade	Mixed	0.715	Tuberculosis
49	4	3,200	Hypothrepsia, 2d grade	Mixed	0.98	Gained 600 Gm. in 20 days
50	21	5,300	Hypothrepsia, 2d grade	Artificial	0.805	Gained 450 Gm. in 28 days
51	3½	2,965	Hypothrepsia, 2d grade	Mixed	1.085	Gained 370 Gm. in 18 days
52	4	2,750	Hypothrepsia, 2d grade	Mixed	0.755	Gained 300 Gm. in 10 days
53	7	4,300	Hypothrepsia, 2d grade	Breast	0.88	Gained 610 Gm. in 17 days
54	4	3,835	Hypothrepsia, 2d grade	Mixed	0.81	Gained 315 Gm. in 15 days

For a more detailed study of the subject, I shall set apart the cases of both tuberculous and syphilitic cachexia and the cases progressing toward recovery, and I shall divide the cases left into groups according to the intensity of the disturbance in nutrition. This intensity is determined (coefficient C) by dividing the present weight of the child by the difference between this and the normal weight. For instance, a hypothreptic infant 4 months old, weighing 3,700 Gm., who at birth weighed 3,000 Gm., when the normal weight is computed according to the previous observations of Nobécourt,[9] should weigh 6,000 Gm.; the present weight, then, is 2,250 Gm. less than normal. Therefore, $C = \frac{3,750}{2,250} = 1.66$. As is clearly understood, the coefficient C represents the intensity of denutrition in relation to the present weight.

But if, above all, a division is made with reference to nutritional factors, one sees the outstanding fact in the different behavior of the dextrose content of the blood in infants that were given cereals and in those that were not. Thus, the group of the first forty cases is divided into two others: (1) infants whose diet contained cereals (observations 1, 20, 24, 25, 26, 27, 38, 39 and 40), and (2) infants whose diets did not include cereals. In the first group, the average blood sugar value was 0.741 mg. per thousand cubic centimeters; in the second it was 0.493.

It follows clearly, therefore, that the addition of cereals to the diet of the hypothreptic infant prevents the fall in blood sugar, which remains close to the normal average, while infants who were not given cereals show accentuated hypoglycemia, the intensity of which is related, as will be seen, to the condition that produces the nutritional trouble.

The dystrophic infants in whose feeding cereals are not included were classified according to the values of coefficient C, and the results of this grouping are as follows:

Coefficient Value	Number of Cases	Average Blood Sugar, Mg.
(1)....less than 1.5	18	0.448
(2)....from 1.5 to 2	5	0.541
(3)....greater than 2	8	0.625

The conclusion drawn from these figures is that the lower the blood sugar, the more accentuated the nutritional disturbance will be.

The last fourteen observations are cachexias of specific syphilitic or tuberculous origin, and cases of hypothreptic infants who were recovering. The average amount of blood sugar in the cases of congenital syphilis investigated is 0.798 mg. per thousand cubic centimeters, and in the cases of tuberculosis, 0.876 mg. The values, as is seen, are

9. Nobécourt, P.: Conférence pratiques sur l'alimentation des nourrissons, ed. 3, Paris, Masson & Cie, 1922, p. 7.

normal. In the case of congenital syphilitic infants fed by breast, it is understood that syphilitic nurses gave them the breast or that they were fed with milk pumped from it.

It is conspicuous that, with very low values for coefficient C, the dextrose content of the blood remains close to the normal value; thus, in the forty-first observation in which coefficient C was 0.72, the blood sugar was 1.02 mg. per thousand cubic centimeters; the diet consisted only of human milk. If one keeps in mind that for values of C lower than 1.5 the average blood sugar value obtained in cases of nutritional dystrophy was 0.448, one must infer that the process leading to athrepsia in the two groups of cases is absolutely different, since in dystrophies resulting from chronic infection, the carbohydrates do not seem to be affected. In six hypothreptic infants on the way to recovery (the last six observations), the average amount of blood sugar was 0.885 mg. per thousand cubic centimeters.

COMMENT

According to our own data, the average dextrose content of the blood in the nutritional cachexias is 0.53 mg. per thousand cubic centimeters. As was noted, my associates and I obtained a figure distinctly lower than the averages given by several investigators. But that is because we considered merely nutritional dystrophies, excluding those of specific origin (syphilitic or tuberculous) in which I have shown that the hypoglycemia characteristic of the former group does not occur; neither does this average include the cases of hypothrepsia in which the patients were on the way to recovery, as these patients present also, as was shown, high normal values for blood sugar. If all these groups should be included in the computation, an average of 0.624 mg. per thousand cubic centimeters is obtained. But our figure is, even then, lower than those of other authors (with the exception of Wilson and his co-workers), and this may, in part, be due to the inclusion of some particularly low figure obtained before and at the agonal stage. When these factors—the cases of cachexia of nonnutritive origin and the unusually low figures—are excluded, an average is finally obtained that is comparable to those obtained by the authors mentioned previously, which reaches 0.656 mg. per thousand cubic centimeters, i. e., a figure 25 per cent lower than the normal average.

If, however, as was done, the complex group of cases of hypothrepsia is dismembered in order to consider only those with a nutritional cause and if these are further subdivided into those with a high blood sugar content, it will be observed that, save for a few exceptions, these high values are found (in the absence of severe complaints) in subjects fed cereals or in hypothreptic infants progressing toward recovery. When these cases are eliminated, there is a group left that

includes extremely hypothreptic babies in whose diet cereals were not included; in this group the blood sugar reaches, according to our own data, an average of 0.493 mg. per thousand cubic centimeters, i. e., a figure 43.9 per cent lower than the normal one.

It is also deduced from our experimental researches that the fall in blood sugar is in relation, to a certain extent, to the intensity of denutrition, which is considered in some degree as an index of the gravity of the dystrophy. Thus, the nearer to the time of death that the determination was made, the lower, in general, was the figure for the blood sugar. In the ten days preceding death, the blood sugar was 0.32 mg. on an average; between ten and twenty days prior to death, it reached an average of 0.47 mg., and more than 30 days before death, the average was 0.57 mg.

The interest of these data is greater because the only alteration clearly confirmed in the carbohydrate metabolism in the dystrophies is the hypoglycemia. In fact, Talbot and Hill [10] and Utheim [11] observed that the absorption of carbohydrates is perfectly achieved by athreptic infants, since they can be administered in large proportions without increasing the amount in the feces. One might well think of an excess of carbohydrate ferments in the intestine; this is true, however, only in cases followed by diarrhea.

Moreover, the organism of the athreptic infant not only absorbs regularly the dextrose that is ingested, but allows it to pass into the blood stream and removes it therefrom in the same time and proportion as does that of healthy infants, as was shown by the blood sugar curves in the experimental work of Brown and Tisdall and their assistants. Brown verified the observation that the highest blood sugar value for athreptic infants does not reach that of normal children, and Tisdall and Brown found, besides, that injected dextrose disappears from the blood stream of athreptic infants quicker than from that of healthy nurslings.

The tolerance of hypothreptic infants for dextrose seems to be even greater than that of healthy infants. Thus, Nobécourt [12] confirmed that the former can ingest at once from 4 to 5 Gm. of dextrose per kilogram of weight without showing higher glycemia, while normal infants cannot ingest more than 3 Gm. per kilogram.

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10. Talbot, F. B., and Hill, L. W.: The Influence of Lactose on the Metabolism of an Infant, with Special Reference to Fat, Nitrogen and Ash, Am. J. Dis. Child. **8**:218 (Sept.) 1914.

11. Utheim, Kirsten: Metabolism Studies in Infants Suffering from Chronic Nutritional Disturbances (Athrepsia), Am. J. Dis. Child. **22**:329 (Oct.) 1921.

12. Nobécourt, P.: La tolérance des nourrissons pour le sucre: Les hautes doses de saccharose chez les bébés cachectiques, Arch. de méd. d. enf. **30**:313, 1927.

Similar, though of greater precision, were the experiments of Matill, Meyer and Sauer,[13] who found increased tolerance for dextrose in the athreptic infant. The average tolerance in seven athreptic infants was from 1.4 to 1.5 Gm. per kilogram per hour (normal, from 0.8 to 0.9 Gm.). Helmholz and Sauer,[14] using Woodyatt's method, found that in six athreptic infants the tolerance for dextrose varied between 1.4 and 1.8 Gm.

However, the seeming increase in tolerance for dextrose in athreptic infants does not really exist, as when calculations are made, not according to the present weight, but according to the metabolically active tissue (as was the method of Tisdall and his co-workers) identical values result for both normal and athreptic babies.

In an interesting work, Wilson, Levine and Gottschall [4] investigated the metabolic capacity of the organism of the athreptic infant for dextrose, determining the increase in the respiratory coefficient after the ingestion of a known amount of carbohydrate. They have discovered that, on the basis of the present weight, athreptic infants burn a greater proportion of dextrose than sound nurslings (0.7 Gm. per kilogram an hour). But when computations are made according to the amount of metabolically active tissue, identical results are obtained in both normal and athreptic infants (0.5 Gm. per kilogram an hour). These authors assume that in normal infants 30 per cent of the body weight is made up of fat tissue, metabolically inactive, and that by multiplying the athreptic baby's weight by $\frac{100}{70}$, one obtains the weight that would have resulted had the body contained the proportional amount of fat. These authors conclude, like those already mentioned, that athreptic infants absorb carbohydrates and metabolize them in the same way as do normal infants.

There remains, then, as the only positive datum on the blood sugar the fact that it is low, having been found to average 0.493 mg. per thousand cubic centimeters.

The similarity of these data to those obtained by Tosi [15] for infants on a fasting stomach is surprising. Determining the dextrose content of the blood in ten children from 1 to 5 years of age during twelve, twenty-four, twenty-eight and fifty-four hours during which they were given only sweetened water, this author showed that in the first thirty-six hours (twenty-four for nurslings) the blood sugar descends to a minimum of from 0.3 to 0.4 mg. per thousand cubic centimeters; after-

13. Matill, P. M.; Mayer, K. M., and Sauer, L. W.: Dextrose Tolerance in Atrophic Infants, Am. J. Dis. Child. **19**:42 (Jan.) 1920.

14. Helmholz and Sauer: Dextrose Tolerance in Atrophic Infants, Tr. Am. Pediat. Soc., 1919.

15. Tosi, G.: Il comportamento della curva glicemia nel bambino, durante il digiuno prolungato, Clin. pediat. **8**:577, 1926.

ward, it ascends a little, reaching about 0.5 mg., at which level it remains. The author attributes this elevation to the fact that the hepatic supply of glycogen has been exhausted and a demand is made on the extrahepatic supply (muscular, etc.) to keep up the minimum threshold. He suggests also the possibility of an excitation of the suprarenal glands through long fasting.

In athrepsia, both the physiopathologic and anatomic data have demonstrated their similarity with the findings in simple starvation of young animals. By this similarity, the decrease in blood sugar parallel with the intensity of the nutritional disturbance may find an explanation. In less marked cases (coefficient C higher than 2) the available supply of hepatic glycogen has not yet been exhausted and the blood sugar remains relatively high (0.625 mg. per thousand cubic centimeters); with the progress of the denutrition, the hepatic supply is exhausted, the organism then making use of the extrahepatic glycogen in order to keep the glycemic index, already so low (C, 1.5 to 2; blood sugar, 0.54 mg.), as high as possible. At last, the process of autophagia, which has already consumed 90 per cent of the fat of the body, destroys the muscular masses (final hyperazotemia [Nobécourt [16]]) and exhausts its supply of glycogen, following which the dextrose content of the blood falls again (C, lower than 1.5; blood sugar, 0.448 mg.). In the final stages the organism of the athreptic infant is unable to maintain even the smallest blood sugar value found in cases of long fasting (from 0.3 to 0.4 mg.), and these patients during their last moments consume hepatic dextrose that is not replaced, so that the blood sugar descends rapidly to an incredibly low value, such as 0.1 mg. per thousand cubic centimeters.

But if one considers a hypothreptic infant without diarrhea, in whom, therefore, the functions of digestion and absorption are performed perfectly, it is necessary to assume, since metabolism of the administered carbohydrates is normal, a primary cause for the decrease in his supply of glycogen leading to hypoglycemia, which is the only demonstrable anomaly in the carbohydrate metabolism.

The study of lesions of the endocrine glands in athrepsia may throw some light on the nature of the primum movens of the hypoglycemia in dystrophic children. In the pancreas in athreptic infants Mattei [17] (quoted by Nobécourt) found an increase in the islands of Langerhans and signs of hyperactivity.

In the suprarenal glands "the lesions plainly prevail in the medullary substance"; the volume and weight of the whole gland are diminished,

16. Nobécourt, P.: Des hypotrophies et des cachexies des nourrissons, Arch. de méd. d. enf. **19**:195, 1916.

17. Mattei, quoted by Nobécourt (footnote 16).

so that it weighs scarcely $\frac{1}{2.000}$ instead of the normal $\frac{1}{750}$ of the weight of the body.

Mattei has found in the thyroid glands of athreptic infants, atrophy, degenerative and parenchymatous lesions and invading sclerosis, severe enough to indicate that there is a striking functional insufficiency.

It is surprising that there is pronounced atrophy of the thymus, accompanied by marked sclerosis, with regression of the parenchyma. The Hassall corpuscles show cystic degeneration.

In short, there are degenerative lesions of the suprarenal glands, thyroid and thymus and signs of hyperactivity of the incretory pancreatic gland.

We know that, schematically, the metabolism of saccharin is submitted to endocrine antagonistic regulative actions represented by the islands of Langerhans and their incretion insulin, which (1) blocks the beginning formation of dextrose from proteins and fats, (2) in a first period, increases the glycogen synthesis in liver and muscles and causes hypoglycemia by the association of both mechanisms and (3) finally (if the nutritious amount of carbohydrates is not sufficient) impoverishes the liver and muscles in glycogen, as with the extraglycogenic source (fats and proteins) cut off glycogen alone must provide for the organic requirements of dextrose.

The suprarenal glands act in an antagonistic way through the medium of epinephrine, which produces hyperglycemia, stimulating the formation of dextrose from hepatic glycogen.

Excision of the thyroid gland increases the sensibility of animals to the action of insulin.[18]

Removal of the thymus of young animals, carried out by Piana,[19] led to a notable decrease in blood sugar. This author inferred that the thymus exercises an action antagonistic to that of insulin in young animals.

From a survey, then, of the facts concerning the lesions of the endocrine glands in athrepsia, it is plainly seen that the logical consequence should be hypoglycemia, as the result of hyperinsulinemia not corrected by the hyperglycemic reflex due to the discharge of epinephrine (because of the deficit of the medullary substance of the suprarenal glands). Besides, functional insufficiency of the thyroid gland sensitizes the organism of the atrophic infant to the action of the excess of insulin. On the other hand, the thymic hypofunction should make the hypoglycemia more marked. Brown [2] has shown that when lesions of the endocrine glands are present, glycogenesis from proteins and fats being barred, hypoglycemia occurs. He has also shown that the addi-

18. Evans, C. L.: Recientes adquisiciones en fisiologia, 1929, p. 344. (Recent Researches in Physiology, Philadelphia, P. Blakiston's Son & Co., 1928.)

19. Piana, G.: Modificazioni della curva glicemica in raporto all'azione del timo, Pediatria **37**:1013, 1929.

tion of 8 per cent of fat to the diet does not affect restriction in the production of blood sugar in the dystrophic infant. Tosi [15] obtained the same results in fasting children. He found that in order to keep the hepatic and extrahepatic supplies of glycogen (and the dextrose content of the blood in consequence) within normal limits, a greater amount of carbohydrates must be included in the diet of the athreptic than of the normal infant. My associates and I confirmed this result by showing conservation of the blood sugar within normal limits in the athreptic infant in whose diet cereals were included.

The practical conclusion drawn from this consideration is that the treatment of athreptic infants with injections of insulin is illogical and not without danger. In fact, with this method one can expect only a more intense depletion of the supply of glycogen, if a sufficient amount of carbohydrates is not given at the same time. Moreover, in infants whose blood sugar is already so low, a little mistake in dosage immediately leads to accidents of hypoglycemia, as has often been noted in athreptic infants, in whom pallor, perspiration and convulsions have been observed when from 1 to 2 units of insulin have been given, notwithstanding a previous administration of 20 per cent (from 40 to 60 Gm.) saccharose solution. The success attributed to insulin is due exclusively, I think, to the administration of carbohydrates that necessarily follows it.

Finally, I think it of interest to call attention to the absence of the classic phenomenon of hypoglycemia in the infants investigated in spite of the fact that the nematic dextrose values were below 0.5 mg. per thousand cubic centimeters and in many cases 0.13 mg.

In his researches, Tosi [15] also did not observe symptoms of hypoglycemia after long fasting, notwithstanding the finding of blood sugar values from 0.3 to 0.35 mg. per thousand cubic centimeters. Ferri [20] obtained in his turn, by ten minutes' irradiation with quartz lamps, a fall in blood sugar to about 0.5 mg. without noticing any symptoms of hypoglycemia. Vitetti,[5] on giving insulin to undernourished infants (followed by dextrose), obtained blood sugar values as low as 0.36 mg. per thousand cubic centimeters without apparent hypoglycemic accidents. Tisdall, Brown, Drake and Cody [21] also called attention to the fact that they did not observe clinical signs of hypoglycemia in infants in whom the administration of insulin (plus dextrose) had caused the blood sugar to fall as low as 0.33 mg. and even to 0.25 mg.

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20. Ferri, U.: L'azione dei raggi ultravioletti sull'apparato glicoregolator dei bambini, Riv. di clin. pediat. **25**:217, 1927.

21. Tisdall, Brown, Drake and Cody: Insulin in the Treatment of Malnourished Infants, Am. J. Dis. Child. **30**:10 (July) 1925; also in Selected Articles from the Department of Paediatrics, University of Toronto, 1929, p. 199.

If one keeps in mind that when the blood sugar of adults falls to 0.7 mg. per thousand cubic centimeters, hypoglycemic accidents due to insulin begin; that when it reaches 0.5 mg., tremor and incontinence of feces are noticed and that when it falls to 0.35 mg., coma occurs, it should be admitted that infants show a remarkable difference from adults in this respect.

It may be granted, then, on the basis of the data cited from various investigators as well as from our own observations, that the blood sugar in infants can reach 0.3 mg. per thousand cubic centimeters without the accidents of hypoglycemia.

The absence of hypoglycemia in athrepsia due to infectious diseases (syphilis, tuberculosis) distinguishes it pathogenically from the merely nutritional form. Baratta,[22] in determining the blood sugar of forty-two children of different ages with tuberculosis in various localizations, found it to be within normal limits. One could infer from this that athrepsia of infectious cause expresses a deficiency in the tissues and the latter a deficiency in the feeding. This belief is confirmed by the failure of treatment with dextrose solutions (Macciotta[6]) for syphilitic or tuberculous athrepsia in contrast to the success that such a method affords in the treatment for merely nutritional athrepsia (Macciotta,[6] Matill, Mayer and Sauer,[13] Helmholz and Sauer,[14] Tisdall, Drake and Brown,[3] Nobécourt[12] and others).

CONCLUSIONS

1. The existence of a blood sugar value that is, on an average, 43 per cent lower than normal is confirmed in simple nutritional cachexias.

2. The intensity of hypoglycemia is in proportion to the denutrition.

3. The presence of hypoglycemia has not been confirmed in dystrophies of specific cause (syphilis, tuberculosis).

4. The blood sugar remains within normal limits in hypothreptic infants in whose diet cereals are included.

5. The blood sugar returns to its normal value when the patient with athrepsia is progressing toward recovery.

6. The blood sugar of nurslings can fall as low as 0.3 mg. per thousand cubic centimeters without clinical signs of hypoglycemia.

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22. Baratta, A.: Ricerche sulla glicemia nell'infezione tuberculare dell'infanzia, Pediatria **36**:806, 1928.

HUMAN MILK STUDIES

X. DAILY AND MONTHLY VARIATIONS IN MILK COMPONENTS AS OBSERVED IN TWO SUCCESSIVE LACTATION PERIODS

BETTY NIMS, A.B.

ICIE G. MACY, PH.D.

HELEN A. HUNSCHER, A.B.

AND

MINERVA BROWN, A.B.†

DETROIT

There have been few detailed and extended observations on the milk of individual women. Knowledge concerning the physiologic changes experienced by woman throughout lactation and the limits of variation in the quantity of the different nutrients in the milk and their significance in the nutritional welfare of the infant is still incomplete. The difficulties involved in such investigations explain the fragmentary nature of observations in this field. The interest and cooperation of three women who secreted sufficient milk to meet the demands of both their infants and the laboratory studies have made it possible for us to make continuous detailed observations on the chemical constituents of breast milk over an extended interval of time. We have attempted to gain further information on the modus operandi of milk secretion through detailed dietary, emotional and physiologic observations on these three subjects, conducting our studies under standardized procedures of milk sampling and analysis.

EXPERIMENTAL PROCEDURE

The subjects of this study were the three women who served as the subjects of previous studies reported from these laboratories. Observations were made at monthly intervals during two successive lactations of subjects 6 and 7 and during one lactation of subject 8. In addition, observations were made on the chemical constituents of breast milk during the consecutive days of the balance of metabolic

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From the Nutrition Research Laboratories of the Merrill-Palmer School and the Children's Hospital of Michigan, now the Research Laboratories of the Children's Fund of Michigan.

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† Deceased.

studies [1]; namely, at the sixth week, and the sixth, eighth and fourteenth months of the lactation period. The balance periods varied from three to ten days in length and included a total of twenty-nine, twenty-seven and twenty-one days for subjects 6, 7 and 8, respectively.

Complete records of the food and fluid intake were made. The food was weighed, sampled and analyzed for calcium, phosphorus and nitrogen; the other food components were calculated. The women were observed in their own homes, and psychologic records [2] were kept. There was no attempt, however, to control their dietaries, activities, etc. As contributors to the Mothers' Milk Bureau of Detroit, they were accustomed to expressing all of their milk manually under supervision. The babies were given their mothers' milk by bottle.

During the experimental studies, the milk was completely expressed from both breasts at periodic four hour intervals during the twenty-four hour day. The six samples of milk were then pooled and analyzed. Approved standardized methods of chemical analysis were employed.[3]

EXPERIMENTAL DATA

Data on the percentage composition of human milk reported by numerous observers demonstrate a wide range of variation among individual women.[4] It is not known, however, whether such differences are consistently characteristic of individual women, or are chaotic and inconsistent in value.

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1. The status of the mineral metabolism of the mothers at different periods in the reproductive cycle, as shown by the calcium and phosphorus balances, has been reported (Donelson, E.; Nims, B.; Hunscher, H. A., and Macy, I. G.: Metabolism of Women During the Reproductive Cycle: IV. Calcium and Phosphorus Utilization in Late Lactation and During Subsequent Reproductive Rest, J. Biol. Chem. **91**:675, 1931), and data on the corresponding nitrogen balances are to be published soon.

2. The technic employed in securing the quantitative emotional data has been discussed elsewhere (Hunscher, H. A.; Vincent, E. L., and Macy, I. G.: The Technique of Securing Quantitative and Coordinated Psychological and Physiological Data on Lactating Women in Their Usual Home Environment, Child Development **1**:15, 1930).

3. The following methods of milk analysis were used in this investigation: the micro-Babcock method for fat; the A. O. A. C. method (analysis of the Official Agricultural Chemists) for total solids; the Kjeldahl method for total nitrogen; the A. O. A. C. method I for separation and determination of casein and albumin; the Schaffer-Hartman method for lactose in lactation A and the calculation of lactose by difference in Lactations B; the Clark method for calcium; the Fiske and Subbarrow method for phosphorus and the Van Slyke method for chlorides. For details see Macy, I. G.; Nims, B.; Brown, M., and Hunscher, H. A.: Chemical Analysis of Milk Representative of the Entire First and Last Halves of the Nursing Period, Am. J. Child. Dis. **42**:569 (Sept.) 1931.

4. Hunaeus: Ueber den Kalkgehalt der Frauenmilch, Biochem. Ztschr. **22**:442, 1909. Hess, A. F., and Helman, F. D.: The Phosphatide and Total Phosphorus Content of Woman's and Cow's Milk, J. Biol. Chem. **64**:781, 1925. Widdows, S. T.; Lowenfeld, M. F.; Bond, M., and Taylor, E. I.: A Study of the Composition of Human Milk in the Later Periods of Lactation and a Comparison with that of Early Milk, Biochem. J. **24**:327, 1930.

Observers have recorded studies on the milk of individual women from day to day throughout the colostral [5] and transitional stages [6] and have reported considerable fluctuation of the various milk constituents. The inconstancy of the composition of breast milk during these initial days of lactation has been attributed to abnormalities in the mammary gland during the process of adjusting itself to the processes of milk secretion [7] and is not indicative, therefore, of the degree of change experienced during the mature period (first to ninth months) after milk flow has become established and regulated.[8]

The fluctuation of some of the milk components during successive days of mature lactation is shown graphically in charts 1 to 5. Variations of fat occur in the milk from day to day, and a characteristic level is maintained for each subject (chart 1), as illustrated in the case of subject 8, whose milk consistently showed higher concentrations of fat than did that of subjects 6 and 7. At the same time, subject 8 elaborated a milk that contained greater amounts of total nitrogen, despite daily fluctuations during lactation (chart 2). Individuality was shown likewise in the secretion of mineral constituents; the milk of subject 6 had appreciably greater amounts of total ash (chart 3) and calcium (chart 4) than did that of subjects 7 or 8. On the other hand, the milk of subject 6 contained the lowest concentration of phosphorus; the milk of subject 7 contained a much greater amount (chart 5). These individual characteristics obtained not only during one lactation period but also during the succeeding lactations of subjects 6 and 7 (table 1). The maintenance of individual characteristics is further demonstrated by analyses of the milk of other women, as shown in table 2.

Chemical studies on the composition of human milk during the mature stage have demonstrated that an individual woman may secrete milk fluctuating widely in composition throughout a single day [9] and

5. Lowenfeld, M. F.; Widdows, S. T.; Bond, M., and Taylor, E. I.: A Study of the Variations in the Chemical Composition of Normal Human Colostrum and Early Milks, Biochem. J. **21**:1, 1927. Schloss, E.: Die chemische Zusammensetzung der Frauenmilch auf Grund neuer Analysen, Monatschr. f. Kinderh. **9**:636, 1911; **10**:499, 1912. Schlossmann, A.: Zur Frage der natürlichen Säuglingsernährung, Arch. f. Kinderh. **30**:288, 1900.

6. Hammett, F. S.: Variations in the Composition of Human Milk During the First Eleven Days After Parturition, J. Biol. Chem. **29**:381, 1917.

7. Provan, A. L.: Studies on Colostrum, Welsch J. Agric. **4**:141, 1928; Chem. Abstr. **23**:1670, 1929.

8. Schlossmann, A.: Weiteres zur Frage der natürlichen Säuglingsernährung, Arch. f. Kinderh. **33**:338, 1902. Bahrdt, H., and Edelstein, F.: Das Kalkangebot in der Frauenmilch, Jahrb. f. Kinderh. **72**:16, 1910. Myers, B.: An Investigation on the Analysis of Human Milk, Brit. J. Child Dis. **24**:249, 1927.

9. Nims, B.; Macy, I. G.; Brown, M., and Hunscher, H. A.: Human Milk Studies: IX. Variations in the Composition of Milk at Four Hour Intervals During the Day and Night, Am. J. Dis. Child., to be published.

TABLE 1.—*The Average Composition of Human Milk Secreted by Individual Women During One and Two Successive Lactation Periods (Per 100 Cc. Milk)*

Date	Month of Lactation	Number of Days	Body Weight, Kg.	Volume, Cc.	Fat, Gm.	Lactose, Gm.	Total Solids, Gm.	Total Nitrogen, Mg.	Casein Nitrogen, Mg.	Albumin Nitrogen, Mg.	Total Ash, Mg.	Calcium, Mg.	Phosphorus, Mg.	Calories
Subject 6														
12/ 2/27	14	10	63.1	1,923	4.8	6.8	12.9	169	57	67	197	30.2	13.1	74.5
Lactation A, mean*				2,600	4.7	7.0	12.6	160	53	55	206	33.1	13.1	74.0
10/31/28	2	4	73.1	3,213	4.2	7.3	12.9	191	..	..	236	38.6	14.8	71.4
2/18/29	6	5	64.9	3,490	3.5	7.1	11.8	158	68	38	220	37.4	11.8	63.2
5/ 7/29	8	5	64.7	3,416	4.0	6.9	12.1	160	64	44	211	34.7	11.2	67.4
10/21/29	14	5	65.5	2,848	4.5	6.8	12.5	155	..	..	195	30.7	12.4	71.8
Lactation B, mean*				3,134	3.9	7.1	12.1	157	62	33	209	36.2	11.2	67.1
Subject 7														
10/25/27	14	10	65.9	1,194	5.2	6.8	13.1	176	50	83	181	23.8	16.6	77.9
Lactation A, mean*				2,000	4.2	7.0	12.1	157	49	64	199	28.8	15.5	70.6
11/24/28	2	4	65.0	2,683	4.1	7.0	12.6	201	87	50	221	36.3	17.2	70.2
3/ 4/29	6	5	63.4	2,458	3.5	7.2	11.9	164	68	41	206	34.1	15.6	64.1
5/14/29	8	5	60.4	2,506	3.6	6.9	11.7	161	66	47	201	33.3	15.4	63.4
11/20/29	14	3	61.8	1,739	4.6	6.9	12.8	159	..	..	174	26.6	17.3	73.0
Lactation B, mean*				2,366	3.5	7.1	11.8	160	70	36	199	32.2	15.1	63.7
Subject 8														
8/26/28	2	4	70.4	1,450	4.5	7.5	13.6	222	..	..	228	31.8	17.0	76.1
1/14/29	6	4	80.4	1,654	5.0	6.8	13.2	189	73	48	201	31.8	14.0	77.1
5/ 9/29	8	5	81.5	1,518	5.5	6.6	13.5	190	71	58	201	29.9	12.7	80.2
9/24/29	14	5	81.4	1,323	6.0	6.7	14.1	186	77	59	186	27.1	12.0	85.6
Lactation B, mean*				1,419	5.0	6.8	13.1	186	69	48	201	30.6	13.4	76.5

* Based on all the analyses made during lactation.

TABLE 2.—*The Composition of Human Milk Secreted by Individual Women During the Early Months of Pregnancy (Per 100 Cc. Milk)*

Subject	Date	Week of Lactation	Volume, Cc.	Fat, Gm.	Lactose, Gm.	Total Solids, Gm.	Total Nitrogen, Mg.	Casein Nitrogen, Mg.	Albumin Nitrogen, Mg.	Total Ash, Mg.	Calcium, Mg.	Phosphorus, Mg.	Chloride, Mg.	Comment
1.....	10/20/25	1	171	4.2	5.0	14.2	407	...	...	193	24.0	29.0	82.0	
	10/28/25	2	350	4.3	4.7	13.7	314	102	127	206	23.0	24.0	41.6	
	12/ 2/25	7	688	4.0	5.8	13.7	234	111	70	206	28.0	15.6	34.0	
2.....	2/25/26	2	409	3.4	6.9	12.0	260	67	110	280	26.6	14.6	61.0	
	3/16/26	5	50	4.2	6.5	14.2	275	...	...	...	....	....	....	
3.....	5/16/26	2	333	5.4	7.7	14.6	344	89	146	287	33.0	21.6	55.5	
	6/13/26	6	640	4.6	8.3	12.7	204	65	115	204	30.9	15.8	44.8	
†H 2.....	1/10/30	3	305	4.9	...	....	277	...	...	303	37.8	17.1	....	
	2/12/30	8	247	5.2	6.8	13.6	227	...	...	232	30.9	13.4	....	
H 6.....	1/16/30	3	450	4.9	7.4	14.4	287	...	...	268	26.9	15.5	....	
	2/12/30	7	199	5.2	7.0	13.9	229	...	...	250	25.6	13.5	....	
H 8.....	2/27/30	9	547	4.8	7.1	13.5	233	...	...	217	30.5	16.1	....	Yeast* 1/28/30
	4/30/30	19	458	5.0	6.9	14.0	218	90	62	205	41.4	16.5	....	
	6/ 5/30	24	532	3.3	7.2	13.2	202	86	66	201	43.7	15.4	....	Yeast* 5/ 3/30
	7/10/30	28	608	3.4	8.6	13.8	187	75	56	190	40.7	14.9	....	
H 14.....	4/10/30	11	375	5.8	9.0	13.9	224	...	...	285	57.0	15.8	....	
	4/30/30	13	324	5.5	9.3	14.0	...	86	73	248	32.5	15.3	....	Yeast* 5/ 3/30
	6/ 5/30	18	248	4.1	7.6	13.7	192	76	66	233	28.7	15.4	....	
H 24.....	6/12/30	4	286	2.9	7.6	12.6	157	75	82	236	15.2	12.1	....	
	7/10/30	7	265	2.0	8.2	12.7	196	59	75	212	14.5	11.6	....	Yeast* 6/20/30
H 23.....	6/12/30	7	527	3.5	7.9	13.3	213	80	64	235	31.5	16.6	....	Yeast* 6/13/30
	7/10/30	11	507	1.8	8.2	12.7	186	65	74	220	31.8	14.6	....	

* Six yeast tablets were given daily.

† Subject numbers prefixed by H are those of Dr. B. Raymond Hoobler.

even within a single nursing period.[10] In spite of this individual variation, the separate milk components follow characteristic daily rhythms similar in the milk of all three women. These data suggest a uniformity in the processes of milk secretion inherent in the physiologic activity of the mammary gland itself. Further, each milk constituent followed a characteristic daily rhythm at a level distinctive to each subject, suggesting that individual peculiarities may exist also in the physiologic activity of the mammary gland.

The composition of the milk has been frequently linked with the age of the mother and the number of pregnancies and lactations she has experienced.[11] A comparison of the successive lactation periods of sub-

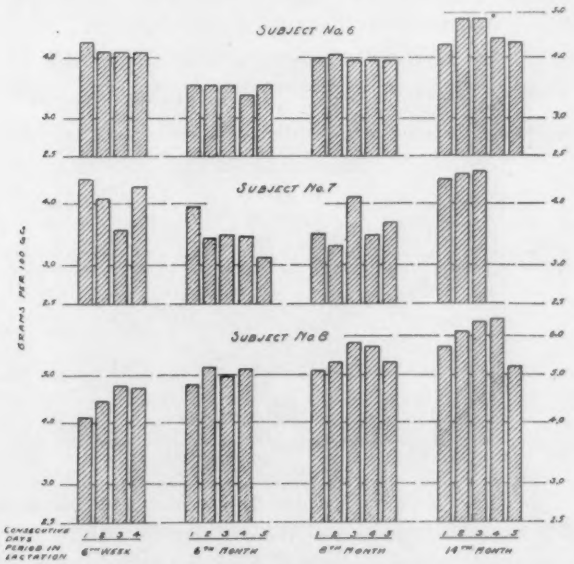

Chart. 1.—The individual differences, the daily variation and the average content of fat in human milk at different periods in lactation, plotted semilogarithmically.

jects 6 and 7 demonstrates a diminished mean value of milk fat in the second lactation, an observation in accord with findings on the cow.[12] The calcium level was appreciably higher in the second lactation, while the mean values of total nitrogen and lactose were approximately the same (table 1).

10. Macy, I. G.; Nims, B.; Brown, M., and Hunscher, H. A.: Human Milk Studies: VII. Chemical Analysis of Milk Representative of the Entire First and Last Halves of the Nursing Period, Am. J. Dis. Child. **42**:569 (Sept.) 1931.

11. Lowenfeld, Widdows, Bond and Taylor (footnote 5, first reference).

12. Glenn, J.; Glenn, M., and Candlish, A. C.: Factors Affecting the Yield and Quality of Milk: II. Variations in Successive Lactations, J. Agric. Sc. **20**:45, 1930.

Constant characteristics are observed in the milk of each woman, even in behavior during chemical analysis. The milk of subject 7 persistently caused difficulty in the precipitation procedure of casein. This observation is in accord with that of Trendtel,[13] who demonstrated individual peculiarities of human milk in the iso-electric point at which casein precipitates. Some milk always demands diacritical temperatures and acid in order to precipitate satisfactorily. Individuality in curd formation has been observed in the milk of cows and has been shown to be a hereditary characteristic.[14]

Various studies on the causes of mineral and vitamin deficiencies in infants have stimulated numerous investigations on the relationship between characteristic diets and milk composition. Our subjects chose adequate, well balanced diets [15] varying individually. Although sub-

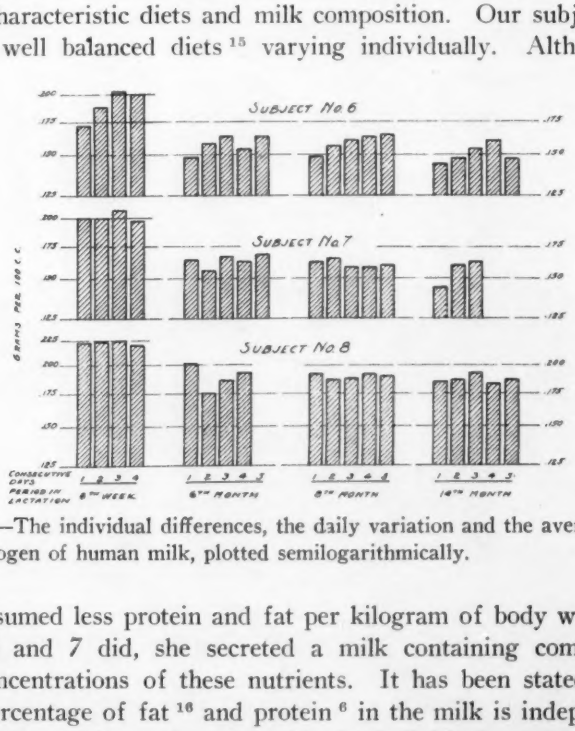

Chart 2.—The individual differences, the daily variation and the average content of total nitrogen of human milk, plotted semilogarithmically.

ject 8 consumed less protein and fat per kilogram of body weight than subjects 6 and 7 did, she secreted a milk containing comparatively greater concentrations of these nutrients. It has been stated that the average percentage of fat [16] and protein [6] in the milk is independent of the plane of nutrition and varies with the individual woman. Studies

13. Trendtel, F.: Ueber individuelle Verschiedenheiten des isoelektrischen Punktes beim Frauenmilchcasein, Biochem. Ztschr. **180**:371, 1927.

14. Hill, R. L.: A Test for Determining the Character of the Curd from Cow's Milk and Its Application to the Study of Curd Variance as an Index to the Food Value of Milk for Infants, J. Dairy Sc. **6**:509, 1923.

15. The diets of these subjects are being reported in detail. (Shukers, C. F.; Macy, I. G.; Donelson, E.; Nims, B., and Hunscher, H. A.: Food Intake in Pregnancy, Lactation and Reproductive Rest in Human Mother, J. Nutrition **4**:399 [Sept.] 1931.)

16. Aurnhammer, A.: Ueber die Beziehungen zwischen Milchproduction und Fettgehalt der Milch, Arch. f. Kinderh. **51**:160, 1909.

made at the eighth month of lactation, after each of the three subjects had taken 15 Gm. of cod liver oil and 10 Gm. of yeast daily throughout the two preceding months, showed better calcium and phosphorus utilization [17] and an increased vitamin B content of the milk [18] as a result of these supplements to the diet. An analysis of the chemical constituents of the milk at the close of this period, however, disclosed no unusual enrichment of the milk. Attention has been focused on the use of vitamin concentrates in increasing the flow and vitamin potency of milk, but there is little evidence that they affect its chemical composition.[19]

The coefficient of variation of the separate milk components has been computed from their corresponding means for each period. A

TABLE 3.—*The Magnitude of Variations of Certain Milk Constituents*

Study	Fat	Lactose	Total Solids	Total Nitrogen	Total Ash	Calcium	Phosphorus
Average coefficient of variation							
During a single day	16.1	4.4	4.4	3.6	3.8	5.5	5.9
From day to day	4.8	3.9	1.3	3.4	2.5	4.5	4.3
Throughout lactation (2d-14th months)	11.1	4.1	3.2	8.9	6.2	8.8	9.2
Average per cent of difference between maximum and minimum							
During a single day	36	11	12	8	11	14	14
From day to day	12	8	3	9	6	11	9
Throughout lactation (2d-14th months)	34	15	11	27	18	27	29
Average per cent of difference between right and left breasts.	0.8	2.1	0.8	1.0	1.7	2.0	2.3
Average per cent of difference between first and last halves of nursing period	26.0	0.2	2.4	8.0	0.8	0.4	7.7

comparison of the magnitude of variations of the milk constituents shows that each of them fluctuates more within a day than from day to day, when twenty-four hour samples are compared (table 3). These figures emphasize that only an analysis of a sample of breast milk representing the twenty-four hour day is significant in determining the nutritive index of milk and that an isolated sample collected at any one hour of the day has little value. It is also evident that averages of several

17. Macy, I. G.; Hunscher, H. A.; McCosh, S. S., and Nims, B.: Calcium, Phosphorus and Nitrogen Utilization in Lactation Before and After Supplementing the Usual Home Diets with Cod Liver Oil and Yeast, J. Biol. Chem. **86**:59, 1930.

18. McCosh, S. S.; Macy, I. G., and Hunscher, H. A.: Human Milk Studies: VI. Vitamin Potency as Influenced by Supplementing the Maternal Diet with Yeast, J. Biol. Chem. **90**:1, 1931.

19. Greiner, I., and Mosonyi, J.: Influence of the Vitamins on the Chemical Composition of Mother's Milk, Am. J. Physiol. **90**:368, 1929; Einfluss der Vitamine auf die chemische Zusammensetzung der Frauenmilch, Jahrb. f. Kinderh. **129**:282, 1930.

successive samples, each representing the twenty-four hour day, must be collected at intervals during the progress of lactation if we are to secure information concerning the gradual changes occurring in the milk of the individual woman during the lactation period.

It has been suggested [20] and demonstrated [21] that the milk of neurotic, high-strung women is less constant in composition than that of even-tempered, phlegmatic mothers. Subject 6 of these studies has been described as a typical high-strung,[22] excitable person, and her sister, subject 8, as of characteristically phlegmatic temperament.[2] As based on the analysis of the milk collected at four hour intervals throughout the day, a high coefficient of variation of milk constituents was found for subject 6,[9] whereas the milk of subject 8 showed greater fluctuation from day to day (table 4), as shown by analysis of the pooled twenty-four

Chart 3.—The individual differences, the daily variation and the average content of total ash in human milk at different periods in lactation, plotted semilogarithmically.

hour samples of milk. These differences in the magnitude of variation of milk constituents of the two subjects may be partly due to the high milk fat of subject 8, since milk of high fat concentration has been noted to exhibit a greater degree of variability in all its constituents.[23]

20. Talbot, F. B.: A Summary of Present Knowledge of Human Milk, Am. J. Dis. Child. **7**:445 (June) 1914. Griffith, J. P. C., and Mitchell, A. G.: The Diseases of Infants and Children, ed. 2, Philadelphia, W. B. Saunders Company, 1927, vol. 1, p. 104.

21. Sisson, W. R., and Denis, W.: Observations on the Salt Content of Human Milk, J. A. M. A. **75**:601 (Aug. 28) 1920.

22. A study of the type and intensity of emotions in relation to the chemical composition of the milk will be reported in the future.

23. Trunz, A.: Ueber die mineralischen Bestandteile der Kuhmilch und ihre Schwankungen im Verlaufe einer Laktationsperiode, Ztschr. f. physiol. Chem. **40**: 263, 1903.

A decrease of milk fat [24] and occasional changes in other constituents, as well as in the quantity of milk,[25] are reported to accompany the occurrence of menstruation in the mother.[26] Colic, indigestion,[27] diarrhea, and even loss of weight in the child [28] have been reported to occur at this time. The figures in table 5 show the values of the milk constituents on the first day of menstruation as compared with the mean values for the three consecutive twenty-four hour days preceding menstruation for subject 8 at the sixty-fifth week of lactation. They show that the deviation of the milk constituents from the mean was no greater on the first day of menstruation than within the three consecutive days just preceding.

TABLE 4.—*The Coefficient of Variation of Constituents in the Milk of Subjects 6, 7 and 8*

Study	Subject	Fat	Lactose	Total Solids	Total Nitrogen	Total Ash	Calcium	Phosphorus	Calories
From day to day.....	6	2.2	2.6	1.4	4.7	3.3	3.2	4.3	1.6
	7	7.1	2.4	1.3	3.1	1.9	5.5	2.7	3.2
	8	4.9	6.2	1.2	2.3	2.4	4.9	5.7	2.5
Throughout lactation (2d-14th months).....	6	10.3	5.1	2.8	9.8	5.9	6.4	10.6	4.8
	7	12.7	2.3	3.7	8.3	6.6	9.6	6.5	5.3
	8	9.5	5.6	3.1	8.5	6.0	12.1	12.0	4.8

TABLE 5.—*Values of Milk Constituents*

	Fat	Lactose	Solids	Total Nitrogen	Ash	Calcium	Phosphorus
Premenstrual period (mean of 3 days).....	5.43	6.78	13.46	0.168	0.184	28.7	11.6
Menstruation (first day).....	5.82	6.77	13.83	0.165	0.186	26.0	11.9

The maximum and minimum values of various food components ingested per kilogram of body weight have been compared with the maximum and minimum values of individual milk constituents. No conspicuous relationship was found in this study between differences in the food intake and fluctuations in the milk composition.

24. Griffith, J. P. C., and Mitchell, A. G.: The Diseases of Infants and Children, ed. 2, Philadelphia, W. B. Saunders Company, 1927, vol. 1, p. 103.

25. Canelli, A. F.: Menstruation et allaitement (observations cliniques—statistiques), Nourrisson **12**:92, 1924. Vertes, O.: Das Verhalten der Menstruation während der Laktation, Zentralbl. f. Gynäk. **52**:1666, 1928. Engel, St.: Laktation und Menstruation, Monatschr. f. Kinderh. **22**:545, 1922. Grulee, C. G., and Caldwell, F. C.: The Influence of Menstruation on Breast Milk, Am. J. Dis. Child. **9**:374 (May) 1915.

26. Rotch, T. M.: Pediatrics, Philadelphia, J. B. Lippincott Company, 1901, p. 144.

27. Hess, J. H.: Feeding and the Nutritional Disorders of Infancy and Childhood, ed. 6, Philadelphia, F. A. Davis Company, 1928, p. 41.

28. Canelli (footnote 25, first reference).

The composition of both human and animal milk has been reported to change gradually with advancing lactation, and average figures are therefore of little value unless the stage in lactation is considered. The general impression has been that there is a gradual but definite decadence in the quality of milk as the cessation of lactation approaches. Most of the data, however, represent average values for many subjects, and there are few data on individual women for an entire lactation period.

The advisability of breast feeding beyond the ninth or tenth months of lactation is questionable. However, though pediatricians do not recommend breast feeding beyond these months, a study [29] of a representative group of American women shows that 42 per cent nursed their babies for six months, 27 per cent for twelve months, 9 per cent for eighteen months and 2 per cent for over two years. The composi-

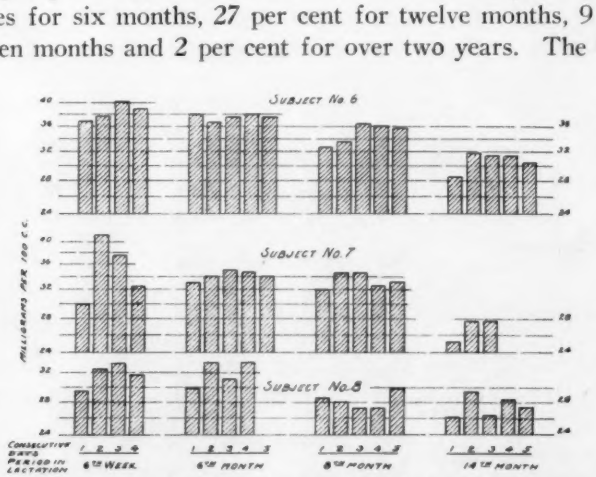

Chart 4.—The individual differences, the daily variation and the average content of calcium in human milk at different periods in lactation, plotted semilogarithmically.

tion of the milk secreted during the months beyond the customary period of breast feeding is, therefore, of both clinical and physiologic significance.

Information concerning the influence of the stage of lactation on the composition of the milk of these women was first sought by means of a series of single twenty-four hour analyses made at monthly intervals in the lactation period. Later, observations were made on consecutive days as representing more adequately the average composition and changes supervening in the milk at the different stages of lactation.

The levels of milk constituents at intermittent intervals in the lactation period, as determined by three day to five day studies, are

29. Mitchell, A. G.: The Duration of the Nursing Period in Women of the United States, J. A. M. A. **66**:1690 (May 27) 1916.

shown in charts 1 to 5 and table 1. There is an appreciable reduction of total nitrogen in the milk of all three subjects from the sixth week to the sixth month of lactation; at the eighth and fourteenth months the levels are approximately the same (chart 2). A gradual decrease in the total nitrogen as lactation progresses has been observed in the milk of both women and cows.[30]

The mean level of lactose seemed to decrease slightly in the milk of subject 6 as lactation progressed, but showed no constant change in the milk of subjects 7 and 8. An increase in lactose with the advance of lactation has been recorded,[31] although occasional observers have reported a decrease,[32] while others have concluded that lactose remains practically constant after the initial stages of lactation.[33] There was a

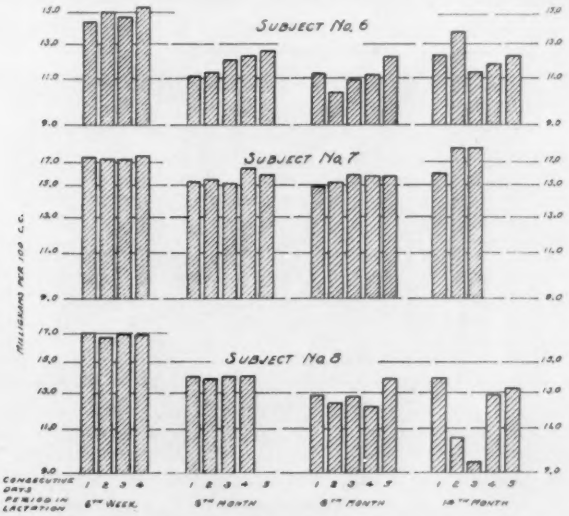

Chart 5.—The individual differences, the daily variation and the average content of phosphorus in human milk at different periods in lactation, plotted semilogarithmically.

30. Pfeiffer, E.: Beiträge zur Physiologie der Muttermilch und ihre Beziehungen zur Kinderernährung, Jahrb. f. Kinderh. **20**:359, 1883. Carter, A. H., and Richmond, H. D.: Some Observations on the Composition of Human Milk, Brit. M. J. **1**:199, 1898. Holt, L. E.; Courtney, A. M., and Fales, H. L.: A Chemical Study of Woman's Milk, Especially It's Inorganic Constituents, Am. J. Dis. Child. **10**:229 (Oct.) 1915. Denis, W., and Talbot, F. B.: A Study of the Lactose, Fat and Protein Content of Women's Milk, ibid. **18**:93 (Aug.) 1919. Gardner, J. A., and Fox, F. W.: On the Variations in the Composition of Normal Human Milk, Practitioner **114**:153, 1925. Bell, M.: Studies on the Composition of Human Milk, J. Biol. Chem. **80**:239, 1928. Schlossmann (footnote 8, first reference).

31. Denis and Talbot (footnote 30, fourth reference). Bell (footnote 30, sixth reference).

32. Carter and Richmond (footnote 30, second reference).

33. Talbot (footnote 20, first reference).

decided decrease of total solids in the milk of all three women from the sixth week to the sixth month, followed by high values at the fourteenth month. The fat content likewise appeared to regain high levels in late lactation. Few investigators have recorded definite conclusions regarding the behavior of fat, although an increase has been suggested in both human milk [34] and cow's milk.[35]

Birk [36] observed high nutrient values in human and cow's milk at the end of lactation. He found that the milk of a woman contained adequate nutrients after three years of continuous milk flow. Raimonde [37] found greater amounts of fat and Schabad [38] increased quantities of lactose in the milk of mothers in late lactation.

The total ash (chart 3) and calcium (chart 4) declined gradually with just perceptible differences between successive intervals. The

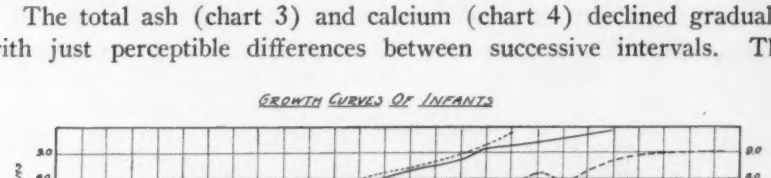
GROWTH CURVES OF INFANTS
BODY WEIGHTS - KILOGRAMS
WEEKS OF LACTATION
INFANT OF SUBJECT No 6
INFANT OF SUBJECT No 7
INFANT OF SUBJECT No 8

Chart 6.—The growth curve of the infants of subjects 6, 7 and 8, plotted semilogarithmically.

phosphorus (chart 5) also decreased during the mature stage but regained a high level at the fourteenth month. The reduction of total ash in human milk as lactation advances has been observed by many

34. Denis, W., and Minot, A. S.: Cholesterol in Milk, J. Biol. Chem. **36**:59, 1918. Fox, F. W., and Gardner, J. A.: The Cholesterol Content of Human Milk, Biochem. J. **18**:127, 1924. Bell (footnote 30, penultimate reference).

35. Ragsdale, A. C., and Turner, C. W.: The Stage of Lactation as a Factor in the Variation of the Percentage of Fat in Cow's Milk, J. Dairy Sc. **5**:22, 1922. Eckles, C. H., and Shaw, R. H.: Variations in the Composition and Properties of Milk from the Individual Cow, U. S. Dept. Agric. Bur. Animal Indust. Bull. 157, 1913.

36. Birk, W.: Zur Frage der Veränderungen der Frauenmilch während des Stillens, Monatschr. f. Kinderh. **25**:30, 1923.

37. Raimonde, R.: Contribution a l'étude chémique du lait de femme (déductions cliniques), Nourrisson **4**:269, 1916.

38. Schabad, J. A.: Der Kalkgehalt der Frauenmilch. Zur Frage der ungenügenden Kalkzufuhr als Ursache der Rachitis, Jahrb. f. Kinderh. **74**:511, 1911.

authors,[39] and occasional reports have indicated a similar decrease in both calcium [40] and phosphorus.[41]

Schloss [42] concluded from his studies on breast milk that the ratio of the components, especially those of total ash and mineral constituents, remained fairly constant, although the absolute values varied greatly. The calcium : phosphorus ratio in the milk of our subjects (table 5) decreased in late lactation, a finding in agreement with those of other observers.[43] The ratio of total ash to total nitrogen remained fairly constant.

It has been suggested that the mammary gland adjusts itself to the nutritive needs of the child, and that there exists a direct relationship between the rate of growth of infants and the rate of decline of various milk constituents. This relationship was first suggested by observations showing that the rate of decrease in the concentration of nutritive building material is proportional to the length of time needed for the young

TABLE 6.—*The Ratio of Certain Milk Constituents at Various Intervals in Lactation*

Month in Lactation	Ca : P			Calcium, per Cent of Ash			Phosphorus, per Cent of Ash			Total Ash : Total Nitrogen		
	Subject			Subject			Subject			Subject		
	6	7	8	6	7	8	6	7	8	6	7	8
A — 14	2.3	1.4	...	15.3	13.1	....	6.6	9.2	...	1.2	1.0	...
B — 2	2.6	2.1	1.9	16.3	16.4	13.9	6.3	7.7	7.4	1.2	1.1	1.0
B — 6	3.1	2.2	2.3	17.0	16.5	15.8	5.4	7.5	6.9	1.4	1.3	1.1
B — 8	3.0	2.2	2.4	16.4	16.5	14.8	5.3	7.7	6.3	1.3	1.3	1.1
B — 14	2.5	1.5	2.3	19.8	15.2	14.5	6.4	9.9	6.5	1.3	1.1	1.0

of a particular species to double its birth weight.[44] Data secured by Telfer [45] indicate that as breast feeding progresses the mineral composi-

39. Carter and Richmond (footnote 30, second reference). Holt, Courtney and Fales (footnote 30, third reference). Gardner and Fox (footnote 30, fifth reference. Bell (footnote 30, penultimate reference).

40. Sikes, A. W.: On the Phosphorus and Calcium of Human Milk, J. Physiol. **34**:464, 1906. Hunaeus (footnote 4, first reference). Schloss (footnote 5, second reference). Bahrdt and Edelstein (footnote 8, second reference).

41. Telfer, S. V.: The Mineral Content of Human Milk in Normal and Rachitic Families, Biochem. J. **18**:809, 1924. Widdows, Lowenfeld, Bond and Taylor (footnote 4, third reference). Schloss (footnote 5, second reference). Sikes (footnote 40, first reference).

42. Schloss (footnote 5, second reference).

43. Widdows, Lowenfeld, Bond and Taylor (footnote 4, third reference).

44. Proscher, F.: Die Beziehungen der Wachsthumsgeschwindigkeit des Säuglings zur Zusammensetzung der Milch bei verschiedenen Säugetieren, Ztschr. f. physiol. Chem. **24**:285, 1897. Aberhalden, E.: Die Beziehungen der Wachsthumsgeschwindigkeit der Säuglings zur Zusammensetzung der Milch beim Hundebeim Schwein, beim Schaf, beim der Ziege und beim Meerschweinchem, ibid. **27**: 408, 1899.

45. Telfer, S. V.: The Mineral Metabolism in Infancy: I. The Mineral Constituents of Human Milk and of Cow's Milk, Glasgow M. J. **113**:246, 1930; II. The Utilization of the Mineral Elements in Human Milk, ibid. **114**:10, 1930.

tion of human milk adjusts itself closely to the needs and mineral retention of the baby. Others have suggested that decreased concentrations of constituents are counterbalanced by increased quantities of milk ingested by the baby.[43] The rate of growth of the infants who were nursed in lactation B of subjects 6, 7 and 8 is shown in chart 6. The curves demonstrate an accelerated rate of growth during the first weeks, followed by a gradual slackening as lactation progresses.

Birk [36] suggested that the increased values of lactose, total solids, and fat in late lactation may be due to some material physiologic changes that stimulate the conditions and composition of the initial colostral and transitional milk and explain the increase in the concentration of milk constituents which accompanies the decrease and cessation of milk flow. There appears to be some uniformity inherent in the physiologic activity of the mammary gland that causes the composition of the milk gradually to change in a definite way as lactation progresses. It has been suggested that the rate of milk secretion is regulated by a monomolecular chemical reaction in which the time factor plays an important rôle.[46]

SUMMARY

Under controlled methods of milk expression, sampling and analysis, extensive observations have been made on three lactating women, two during two successive lactations of fourteen months' duration and a third during a single lactation period of similar duration. Observations were also made on another group of women during the earlier months of lactation.

The nitrogen content of the milk decreased rapidly up to the sixth month and then remained fairly constant; the concentration of total ash and calcium decreased gradually; the phosphorus diminished gradually until the later months, when an increase occurred; the fat and total solids also decreased during the earlier months of lactation and then regained high values in late lactation.

The data demonstrate that the various milk components, although varying from day to day and changing during lactation, fluctuate about a level that is characteristic for the individual woman, and that this individuality of fluctuation is maintained not only during one lactation but also through successive lactation periods. Over and above these individual trends in fluctuation, the composition of the milk in all three subjects showed a similar trend of changes as lactation progressed.

46. Brody, S.; Ragsdale, A. C., and Turner, C. W.: The Rate of Decline of Milk Secretion with the Advance of the Period of Lactation, J. Gen. Physiol. **5**:441, 1923. Gaines, W. L., and Davidson, F. A.: Rate of Milk Secretion as Affected by Advance in Lactation and Gestation, Univ. Illinois Agric. Exper. Sta. Bull. 272, 1926.

THE LEVINSON TEST IN TUBERCULOUS MENINGITIS

MORRIS GLEICH, M.D.
WITH THE TECHNICAL ASSISTANCE OF DR. A. HARTSTEIN
NEW YORK

The Levinson test [1] of the spinal fluid is used to help in making the diagnosis in cases in which tuberculous meningitis is suspected. Frequently one is unable to find tubercle bacilli in the spinal fluid. In the absence of autopsy and inoculation into guinea-pigs one relies primarily on the history, physical findings and clinical data. Additional tests are therefore welcome.

The Levinson test is based on the principle that protein in meningitic spinal fluid reacts electronegatively or electropositively in the presence of certain alkaloid or metallic precipitants. If one adds 3 per cent of sulphosalicylic acid solution (alkaloid precipitant) to epidemic cerebrospinal meningitic fluid (acid in reaction), the protein becomes electropositively charged (cataphoresis to cathode). If 1 per cent solution of mercuric chloride (metallic precipitant) is added to tuberculous meningitic spinal fluid (alkaline in reaction), the protein becomes negatively charged (cataphoresis to anode).

The H-ion concentration of the spinal fluid is an important factor in this test. The reaction of tuberculous and nonmeningitic spinal fluid is alkaline (p_H 7.4 to 7.6), while that of epidemic cerebrospinal meningitic fluid is acid (p_H 7.3 to 7.4) and its acidity increases on standing. The addition of serum (used in the treatment for suppurative types of meningitis) to spinal fluid or the presence of blood therein renders it alkaline. A Levinson test done on this spinal fluid will be positive (table 2). This test must not be made on spinal fluid containing blood or serum.

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From the Pediatric Department of Harlem Hospital.

1. Levinson, A.: The Hydrogen-Ion Concentration of Cerebro-Spinal Fluid, J. Infect. Dis. **21**:556 (Dec.) 1917. Tashiro, S., and Levinson, A.: Alkaloidal and Metallic Precipitation of Cerebrospinal Fluid in the Diagnosis of Meningitis, J. Infect. Dis. **21**:571 (Dec.) 1917. Levinson, A.: Cerebrospinal Fluid in Health and Disease, St. Louis, C. V. Mosby Company, 1919. McQuarrie, I., and Shohl, A. T.: A Colorimetric Method for the Determination of the p_H of Cerebrospinal Fluid, J. Biol. Chem. **66**:367 (Dec.) 1925. Hurwitz, S. H., and Tranter, C. L.: On the Reaction of Cerebrospinal Fluid, Arch. Int. Med. **17**:828 (June) 1916.

TABLE 1.—*Cases of Tuberculous Meningitis with a Positive Levinson Test*

Name Age Color	History and Clinical Data	Spinal Fluid				Levinson Test, Mercuric Chloride Sulphosalicylic Acid*	Pirquet and Mantoux Tests	Roentgen Examination	Diagnosis and Comment
		Reaction	Consistency	Tubercle Bacilli	Cell Count, etc.				
M. B. 6 yrs. Colored	Projectile vomiting; drowsiness; headache; abdominal pains; loss of weight	Alkaline	Clear	.....	Globulin ++; sugar +; 40-60 cells; polymorphonuclears 44 per cent, lymphocytes 56 per cent	Positive weak	Negative	.....	Tuberculous meningitis; patient died
E. O. 2½ yrs. White	Apathy three weeks; coma; headache; photophobia; projectile vomiting; rigid neck	Alkaline	Clear	.....	Globulin ++; sugar —; 40-130 cells; lymphocytes 80 per cent, polymorphonuclears 20 per cent	Positive weak	Positive	Infiltration of right hilus; tuberculous infection	Tuberculous meningitis
M. H. 4 mos. Colored	Ill four weeks; cough, fever, convulsions for 4 weeks; increasing hydrocephalus; coma, consolidation in right lung posteriorly; mother died of tuberculosis	Alkaline	Clear	.....	Globulin ++; sugar +; 80-100 cells; polymorphonuclears 40 per cent, lymphocytes 60 per cent	Positive weak	Negative	.....	Tuberculous meningitis; patient died
E. R. 17 mos. White	Drowsiness one week followed by convulsions; progressing drowsiness and apathy; unconscious on admission; father has tuberculosis	Alkaline	Clear	.....	Globulin ++; sugar —; 1,100 cells; polymorphonuclears 20 per cent, lymphocytes 80 per cent	Positive weak	.....	Increased markings through right upper pulmonary field; suspected early tuberculosis	Tuberculous meningitis; patient died
L. C. 2 yrs. Colored	Pain in neck following gland incision (tuberculous glands); convulsions with muscular twitching; right cervical adenitis (broken down); right strabismus; drowsiness; ptosis of left lid; Brudzinski's sign; Biot's respiration	Alkaline Alkaline	Clear Clear	.....	Globulin +; sugar —; 150 cells; lymphocytes predominating	Positive weak Positive weak	2+ Mantoux 1+ von Pirquet	.....	Tuberculous meningitis
W. N. 18 mos. Colored	Drowsiness; loss of appetite; projectile vomiting; convulsive movements of extremities; rigidity of neck; pupils dilated; do not react to light; slight strabismus; Kernig, Babinski, Brudzinski signs, positive; lungs show finely disseminated crepitating râles; bronchial breathing; tonic spasm upper lobe of right lung	Alkaline	Clear	.....	Globulin +; sugar 0; 150 cells; lymphocytes predominating	14 mm.-4 mm. weak	Negative	Bronchopneumonia	Tuberculous meningitis

B. M. 8 yrs. Colored	Drowsiness; rigid neck; comatose; pupils do not react to light; abdomen scaphoid; marked convulsive and movements of extremities and jactitation; extremities flaccid	Alkaline	Clear	.....	Globulin 0; sugar 0; 50 cells; increased pressure; lymphocytes predominating	5 mm.-2 mm. weak	Negative	.....	Autopsy: acute miliary tuberculosis and tuberculous meningitis
Mc.M. 11 yrs. Colored	Abdominal pain; headache for four months; photophobia; lassitude; fever for ten days; loss of weight; no appetite	Alkaline	Clear	Positive	Globulin 2; sugar +; 180 cells; lymphocytes predominating	Positive weak	.....	Increased markings in right lung	Tuberculous meningitis; patient died
P. W. 13 mos. Colored	Repeated convulsions for one week prior to admission; admitted in coma	Alkaline	Clear	.....	Globulin 2+; sugar 0; 150 cells; lymphocytes predominating	Positive weak	Mantoux positive	.....	Autopsy showed caseous hilus and tracheobronchial glands; tuberculous pneumonia in middle lobe of right lung; tuberculous meningitis
E. T. 4 yrs. Colored	Rigid neck; right pupil sluggish to light; Kernig sign positive; spastic extremities; amaurotic; Brudzinski sign positive; papilledema, 2 diopters; hazy disks	Alkaline	Clear	.....	Globulin 2+; sugar +; 80 cells; lymphocytes predominating	Positive weak	.....	Miliary tuberculosis	Tuberculous meningitis; patient died
A. S. P. 6 yrs. Colored	Vomiting with convulsions; spastic paralysis of left side of body; rigid neck; latent nystagmus; tremor of left extremities; left facial paralysis; eyegrounds normal	Alkaline Alkaline Alkaline	Clear Cloudy Cloudy	.....	Pellicle	8 mm.-2 mm. weak 14 mm.-5 mm. strong 21 mm.-6 mm. weak	Negative	.....	Autopsy: tuberculoma of midbrain
E. M. 11 yrs. Colored	Headache; vomiting; coma; rigid neck, positive Kernig sign; cannot be roused; left pupil larger than right; pupils do not react to light	Alkaline Alkaline	Clear Clear	.....	Globulin 2+; 100 cells; lymphocytes predominating	Positive weak Positive weak	.....	.....	Tuberculous meningitis; patient died
A. G. 2½ yrs. Colored	Convulsions; coma; positive Kernig sign; neck rigid; scaphoid abdomen; positive Brudzinski sign; pupils dilated and fixed, do not react to light	Alkaline	Clear	.....	Globulin 2+; sugar 0; 200 cells; lymphocytes 65 per cent, polymorphonuclears 35 per cent	Positive weak	von Pirquet positive Mantoux positive	.....	Tuberculous meningitis; patient died
I. C. 27 yrs. Colored	Headache; anorexia; loss of weight; infiltration and cavitation in upper lobe of left lung; crepitating râles	Alkaline	Clear	Positive	Globulin 2+; sugar 0; 180 cells; polymorphonuclears 50 per cent; lymphocytes 50 per cent	Positive weak	.....	Tuberculous cavitation in upper lobe of left lung	Tuberculous meningitis; patient died

TABLE 1.—*Cases of Tuberculous Meningitis with a Positive Levinson Test—Continued*

Name Age Color	History and Clinical Data	Spinal Fluid					Pirquet and Mantoux Tests	Roentgen Examination	Diagnosis and Comment
		Reaction	Consistency	Tubercle Bacilli	Cell Count, etc.	Levinson Test, Mercuric Chloride Sulphosalicylic Acid			
J. F. 19 yrs. Porto Rican	Cough; fever; headache; vomiting; dulness over apex of right lung with fine subcrepitating râles; subcrepitating râles in apex of left lung; neck rigid; positive Kernig and Babinski signs; opisthotonos; colloidal gold curve meningitic	Alkaline	Clear	Positive	Globulin 2+; sugar 0; 400 cells; polymorphonuclears predominating	11 mm.-3 mm. weak	.....	Bilateral tuberculosis of lungs	Autopsy: tuberculous meningitis; tuberculosis of lungs
M. F. 6 yrs. Colored	Whooping cough since June, 1930; convulsions with fever; drowsiness; rigid neck; vomiting; bilateral Kernig sign; Brudzinski sign positive	Alkaline Alkaline	Clear Xanthous	.....	Globulin 2+; sugar 0; 1,940 cells; polymorphonuclears 59 per cent, lymphocytes 51 per cent	Positive weak Positive weak	.....	.....	Froin syndrome; tuberculous meningitis; patient died
T. S. 30 yrs. White	Headache; delirium; tremor of extremities; increased deep reflexes; bilateral Kernig sign; Chadwick sign positive; loss of weight; ankle clonus; pulmonary tuberculosis; scaphoid abdomen; semi-comatose; left facial paralysis; irrational; blood and spinal fluid Kahn tests negative	Alkaline Alkaline	Clear Cloudy	Positive	Globulin — +; sugar +; 160 cells; polymorphonuclears 45 per cent	12 mm.-5 mm. weak 24 mm.-8 mm. strong 20 mm.-6 mm. weak 21 mm.-6 mm. strong	.....	Pulmonary tuberculous cavitation in both lungs	Tuberculous meningitis; patient died
J. P. 31 yrs. Porto Rican	Loss of weight; headache; incoherent speech; lungs show crepitating râles at both infraclavicular and interscapular regions; spinal fluid and blood Kahn tests negative	Alkaline	Clear	Positive	Globulin +; sugar +; 100 cells; lymphocytes 60 per cent, polymorphonuclears 40 per cent	16 mm.-4 mm. weak	.....	.....	Autopsy: miliary tuberculosis of brain cord, meninges and other organs
J. C. 33 yrs. Colored	Headache; rigid neck; disorientation; scattered râles throughout both lungs; incoherent speech; spinal fluid Kahn test negative	Neutral	Clear	Positive	Globulin +; sugar +; 50 cells; lymphocytes predominating	9 mm.-4 mm. weak	.....	Miliary tuberculosis	Miliary tuberculosis; tuberculous meningitis; patient died

K. M. 21 yrs. Colored	Neck rigid; pain in occipital region; reflexes sluggish; blood Kahn test negative; Babinski and Kernig signs negative; spinal fluid Kahn test negative	Neutral	Clear	Positive	Globulin +; sugar —; 200 cells; mononuclears predominating	12 mm.-3 mm. weak 6 mm.-2 mm. strong	.....	.....	Tuberculous meningitis; patient died
W. S. 10 yrs. Colored	Abdominal pain; headache; scaphoid abdomen; very toxic; rigid neck; bilateral Kernig sign; Brudzinski sign positive; spasm of left side of face; fungi negative; diminished reflexes of lower extremities	Alkaline Alkaline Alkaline	Clear Clear Clear	....	Globulin 2+; sugar 0; 250 cells; lymphocytes 60 per cent, polymorphonuclears 40 per cent	12 mm.-4 mm. weak 12 mm.-4 mm. strong 12 mm.-4 mm. weak 16 mm.-4 mm. strong 18 mm.-6 mm. weak 19 mm.-6 mm. strong	.....	Lungs negative for tuberculosis	Tuberculous meningitis; patient died
J. L. 2 yrs. Colored	Fever; headache; vomiting (projectile); convulsions; drowsiness; rigid neck; apathy; positive Brudzinski sign; bilateral Kernig sign; internal strabismus of right eye; left facial paralysis	Alkaline Alkaline Alkaline	Clear Clear Clear	....	Globulin +; sugar 0; 250 cells; polymorphonuclears 55 per cent, lymphocytes 45 per cent	8 mm.-3 mm. weak 8 mm.-4 mm. strong 4 mm.-2 mm. weak 7 mm.-2 mm. strong 4 mm.-0 mm. weak 5 mm.-2 mm. strong	Negative	.....	Tuberculous meningitis; patient died
A. P. 21 yrs. Porto Rican	Vomiting; convulsive movements of left side of body; pupils dilated and fixed; comatose; eyegrounds normal	Alkaline	Clear	Positive	Globulin 4+; sugar 0; 100 cells; polymorphonuclears 60 per cent, lymphocytes 40 per cent	14 mm.-2 mm. weak 14 mm.-4 mm. strong	.....	.....	Autopsy: tuberculous meningitis
F. R. 11 yrs. Porto Rican	Admitted in semicomatose state; pupils fixed; bilateral Kernig sign; right upper extremity rigid; spasm of left side of face; paralysis of right side of face; scaphoid abdomen; right hemiplegia; spinal fluid Kahn test negative	Alkaline	Clear	.....	Globulin +; sugar +; 200 cells, mononuclears predominating	9 mm.-3 mm. weak 8 mm.-2 mm. strong	.....	Lungs normal	Tuberculous meningitis; patient died
I. R. 33 yrs. Colored	Onset two months previously; insidious; rigid neck; headache; abdominal pain; poor appetite; stupor; pupils sluggish to light	Alkaline	Clear	Positive	Globulin 2+; sugar +; 50 cells; polymorphonuclears 50 per cent, lymphocytes 50 per cent	9 mm.-4 mm. weak	.....	Miliary tuberculosis	Autopsy: tuberculous meningitis; miliary tuberculosis

* In this column, weak = 1 per cent hydrochloric acid solution plus 3 per cent sulphosalicylic acid solution; strong = 2 per cent hydrochloric acid solution plus 6 per cent sulphosalicylic acid solution.

TABLE 2.—*Cases Showing a Positive Levinson Test After the Administration of Serum*

Name Age Color	History and Clinical Data	Spinal Fluid					Serum	Roentgen Examination	Diagnosis and Comment
		Reaction	Consistency	Micro-Organisms	Cell Count, etc.	Levinson Test, Mercuric Chloride Sulphosalicylic Acid			
D. T. 1½ yrs. Colored	Drowsiness; vomiting; rigid neck; bilateral Kernig sign; positive Brudzinski sign; opisthotonos; bilateral otitis media; (purulent); comatose; abscess on big toe; right internal strabismus	Alkaline Alkaline Alkaline Alkaline	Cloudy Cloudy Cloudy Cloudy	Gram-negative bacillus	Globulin 2+; sugar +; 610 cells; polymorphonuclears 85 per cent, lymphocytes 15 per cent	0 mm.-2 mm. weak 2 mm.-5 mm. strong 6 mm.-3 mm. weak 8 mm.-3 mm. strong 0 mm.-0 mm. weak 9 mm.-3 mm. strong 3 mm.-3 mm. weak 6 mm.-3 mm. strong	None Serum Serum Serum Serum Serum	Mastoids normal	Influenzal meningitis; autopsy showed: base of brain covered with greenish-yellow exudate, showing influenzal organisms on smear and culture; Parke Davis influenzal serum given
S. P. 4 yrs. Colored	Drowsiness; headache; vomiting; rigid neck, staggering gait; Babinski and Brudzinski signs positive; petechiae on chest; opisthotonos; internal strabismus (bilateral)	Alkaline Alkaline Alkaline	Cloudy Cloudy Cloudy	Gram-negative diplococcus, intracellular	Globulin 2+; sugar +; 500 cells; polymorphonuclears 85 per cent	6 mm.-8 mm. weak 8 mm.-5 mm. strong 2 mm.-2 mm. weak 6 mm.-3 mm. strong 4 mm.-4 mm. weak 7 mm.-4 mm. strong	None Serum Serum Serum Serum Serum	.....	Meningococcus meningitis
J. W. 19 yrs. Colored	Headache; rigid neck; fever; vomiting; cough; positive Brudzinski and Kernig signs	Acid	Cloudy	Pneumococcus, type 3	Globulin 3+; sugar 0; 2,200 cells; polymorphonuclears 87 per cent, lymphocytes 13 per cent	Positive weak	Serum	.....	Pneumococcus type 3; meningitis; type 3 pneumococcus serum given
M. J. 3 yrs. Colored	Otitis media (chronic, purulent, right) for three months; one week later child fretful; hemorrhage of conjunctivae; vomiting; rigid neck; lungs clear; Brudzinski sign positive; Babinski sign negative; fundi normal; suggestive Kernig sign on left; both ear drums gray and opaque, no bulging; positive McEwen sign over right parietal region	Alkaline	Cloudy	Gram-negative bacillus	Globulin 3+; sugar 0; 2,000 cells; polymorphonuclears 90 per cent, lymphocytes 10 per cent	Positive weak Positive weak	Serum Serum	Mastoids normal	Autopsy showed changes; brain abscess in right temporal lobe; pus showed influenza bacillus; influenzal meningitis; Parke Davis influenzal serum used
H. A. 25 yrs. Colored	Opisthotonos; headache; rigid neck; Kernig and Brudzinski signs positive; Oppenheim and Gordon signs positive	Alkaline	Cloudy	Gram-negative bacillus	Globulin 3+; sugar 0; 1,500 cells	Positive weak	Serum	.....	Meningococcus meningitis

The Levinson test is done thus: One cubic centimeter of spinal fluid is placed in each of the two test tubes 8 mm. in diameter. To one is added 1 cc. of a 1 per cent solution of mercuric chloride and to the other, 1 cc. of a 3 per cent solution of sulphosalicylic acid. The tubes are well shaken, stoppered and allowed to stand at room temperature for forty-eight hours. At the end of twenty-four and forty-eight hours the column of precipitate in each tube is measured in millimeters. When the height of the precipitate in the first test tube is seen to be twice that of the precipitate in the second tube, the result of the test is positive.

We felt at one time that a ratio of 2:1 was not sufficiently pathognomonic of tuberculous meningitis. We suggested increasing the height of the precipitate in each test tube and reporting it in millimeters rather than stating in a general way that the Levinson test is positive on the basis of the 2:1 ratio. We thought that this method of reporting the test was more accurate and would give fewer positive Levinson tests in nonmeningitic spinal fluids. A glance at table 3 shows several cases of nontuberculous meningitis with alkaline spinal fluid and a ratio of 2:1 or more. Pons [2] had already reported six cases of cerebrospinal syphilis in twenty-four with a ratio of 2:1 or more and had suggested the use of stronger solutions. We therefore decided to use stronger solutions, e. g., a 2 per cent solution of mercuric chloride and a 6 per cent solution of sulphosalicylic acid. After several tests we noted that stronger solutions did not yield more accurate results. The ratio of precipitates in cases of nontuberculous (see table 3) and tuberculous (table 1) meningitis did not vary. We therefore abandoned stronger solutions. We must conclude that the present method of reporting a positive Levinson test—e. g., the precipitate in the test tube containing mercuric chloride twice that of the precipitate in the test tube containing sulphosalicylic acid—is ample.

Occasionally one encounters a positive Levinson test in cerebrospinal syphilis, general arteriosclerosis with or without brain hemorrhage, amyotrophic lateral sclerosis or uremic coma associated with hypertension and nephritis (table 3). In such cases, however, a careful history, a thorough physical examination and clinical data will easily rule out tuberculous meningitis. One does not discredit the Wassermann test because it is occasionally found to be positive in tuberculosis. One insists on finding organic pathologic conditions indicative of syphilis before considering a positive Wassermann reaction in a case of tuberculosis. The same should be true of the Levinson test.

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2. Pons, C. A., and Fletcher, T. A.: The Levinson Test and Other Laboratory Studies in Tuberculous Meningitis: The Human Cerebrospinal Fluid, New York, Paul B. Hoeber, Inc., 1924, vol. 4.

TABLE 3.—*Group III. Miscellaneous Cases (Bloody Spinal Fluid, Etc.) with Positive Levinson Test*

Name Age Color	History and Clinical Data	Spinal Fluid: Reaction	Spinal Fluid: Consistency	Spinal Fluid: Micro-Organisms	Spinal Fluid: Cell Count	Levinson Test, Mercuric Chloride Sulphosalicylic Acid	Roentgen Examination	Diagnosis and Comment
E. C. 45 yrs. Colored	Paralysis of right side; unable to walk; vision poor; "pins and needles" in right arm for three years; pupils sluggish to light; blood Kahn test 4+; spinal fluid Kahn test negative; colloidal gold test showed syphilitic curve	Alkaline	Clear	.....	Globulin 2+; sugar, trace; 15 cells	Positive weak	.....	Cerebrospinal syphilis; patient discharged
M. P. 50 yrs. Colored	Onset one year previous with headache, dizziness and fainting spells; mild left facial paralysis; pupils irregular, did not react to light; rigid neck; bilateral Kernig and Mosenthal signs positive; blood pressure, 210 systolic and 110 diastolic; spinal fluid Kahn and blood Kahn test negative	Alkaline	Bloody	.....	.....	11 mm.-3 mm. weak	.....	Essential hypertension; cardionephritis; subdural hemorrhage; patient discharged
W. A. T. 40 yrs. Colored	Headache; pain in the neck; vomiting; drowsiness; delirium; no fever; moderate rigidity of neck; bilateral Kernig sign; left hemiplegia; blood pressure 180 systolic and 110 diastolic; colloidal gold curve meningitic; spinal fluid and blood Kahn tests negative	Alkaline	Bloody	.....	.....	8 mm.-6 mm. weak 18 mm.-8 mm. strong	No skull fracture	Subdural hemorrhage; arteriosclerosis
R. U. 40 yrs. Colored	Patient admitted in coma; left hemiplegia; blood pressure 210 systolic and 70 diastolic; eyegrounds showed tortuous vessels; pupils did not react to light; slight rigidity of neck	Alkaline	Bloody	.....	.....	9 mm.-3 mm. weak 8 mm.-2 mm. strong	.....	Subdural hemorrhage; arteriosclerosis; chronic nephritis
F. M. 56 yrs. Colored	Headaches for a year; patient attended clinic for syphilitic treatment; unable to talk; right facial paralysis; pupils did not react to light; tongue protruded to right; scar on glans penis; scar in right inguinal region; mentally abnormal; blood and spinal fluid Kahn tests negative; eyegrounds show right choroiditis; failing vision	Alkaline	Clear	.....	Globulin 0; sugar +; 10 per cent mononuclears	8 mm.-2 mm. weak 7 mm.-2 mm. strong 6 mm.-2 mm. weak	Encephalogram shows cortical atrophy; lungs normal; skull showed no neoplasm	Cerebrospinal syphilis; patient discharged
J. F. 45 yrs. Porto Rican	Progressive weakness; frontal headache for one month; loss of function of left arm and left leg; chest clear; pupils sluggish and irregular; spinal fluid Kahn test negative	Neutral	Clear	.....	Globulin 0; sugar 0; 10 cells	9 mm.-4 mm. weak	.....	Left hemiplegia; cerebrobrospinal syphilis
C. J. 33 yrs. Colored	Onset nine days previous with headache, fever of septic type and cough; patient lethargic on admission; fundi normal; neck stiff; white blood cells 9,000; polymorphonuclears 74 per cent; lymphocytes 26 per cent; lungs clear; Babinski and Brudzinski signs positive; blood Kahn test 2+; Widal stools negative for typhoid; colloidal gold curve syphilitic	Alkaline Alkaline	Clear Clear	.....	Globulin +; sugar +4; 45 cells	14½ mm.-4 mm. weak	.....	Grip; meningismus cerebrospinal syphilis; patient discharged
R. M. 45 yrs. White	Voluntary movements of lower extremities poor; loss of weight; emaciation; extremities showed wasting; muscle wasting all over body; patient unable to walk; loss of power in upper extremities; lungs clear; asthenia; pain in calf of muscle; blood Kahn test negative; colloidal gold curve showed syphilitic zone; spinal fluid Kahn test negative	Alkaline Alkaline	Clear Clear	....	....	Positive weak Negative weak	....	Amyotrophic lateral sclerosis

We consider that the Levinson test is of value. Days before tubercle bacilli were found in the spinal fluid, if at all, or autopsies helped to confirm the diagnosis, the Levinson test was positive. In all of the cases of tuberculous meningitis the test was positive. In these cases the finding of tubercle bacilli or autopsy confirmed the reliability of the Levinson test. However, the test is corroborative and should be considered together with the history, physical findings and clinical data in making a diagnosis.

fluid Kahn test negative

SYMPTOMS IN CONGENITAL LESIONS OF THE HEART THAT PERMIT VENOUS SHUNTING

CLIFTON BRIGGS LEECH, M.D.
PROVIDENCE, R. I.

Among eighty-two instances of congenital heart disease collected from the Johns Hopkins Hospital autopsy records, there were sixty-two of such a nature as to permit a direct admixture of venous with arterial blood through an abnormal communication within the heart or great vessels. A flow of blood from the right to the left side of the heart through such a defect is designated as a venous shunt. The venous shunt types of defects in these patients were usually associated with other congenital lesions of the heart. The following summary of the lesions shown in these sixty-two patients does not include the complicating abnormalities:

Patent ductus arteriosus (uncomplicated)	17
Patent ductus arteriosus plus patent foramen ovale	19
Patent ductus arteriosus plus defect in interventricular septum	3
Patent ductus arteriosus plus defect in interventricular septum plus patent foramen ovale	3
Patent ductus arteriosus plus other defects not of the venous shunt type	4
Patent foramen ovale (widely patent)	2
Defect in interventricular septum	8
Patent foramen ovale plus defect in interventricular septum	4
Patent foramen ovale plus defect in interauricular septum	1
Defect in interventricular septum plus defect in interauricular septum	1
	62

The clinical records of these patients were studied in an attempt to determine whether such abnormal communications between the venous and arterial circulations produced characteristic symptoms and signs. It must be stated here that a number of the instances of patent ductus arteriosus were in infants who died at such an early age that there can be no certainty that the lesion did not represent a mere delay in closure of the ductus rather than a true congenital defect. Although in this series cases of widely patent ductus arteriosus only were included, at very early ages it is difficult for the pathologist to deter-

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From the Department of Pediatrics, Johns Hopkins University School of Medicine, and the Harriet Lane Home, Johns Hopkins Hospital.

mine whether or not an actual malformation is present. Some authorities think that delay in closure up to several weeks or months is not uncommon, and that patency of the ductus arteriosus is found frequently at autopsies of very young infants. It would seem to make little difference whether the patency represents a true congenital anomaly or merely a delay in closure, since the functional disturbance may result in the production of similar signs and symptoms in either case.

Nearly half (43 per cent) of the sixty-two patients showed nothing in life to suggest any sort of congenital lesion of the heart. In an additional 16 per cent, the signs and symptoms were of little diagnostic value. Cyanosis was absent in thirty-one (50 per cent), constantly present in about 24 per cent of the group and appeared as a temporary or periodic sign in approximately 26 per cent. Among the group of twenty patients with lesions that did not allow venous shunting, cyanosis was absent in 65 per cent, constantly present in 20 per cent and periodic or temporary in 15 per cent, approximately. Many of the sixty-two patients in the main group also had other congenital abnormalities of the heart, which may have played a part in the production of the cyanosis. Consequently, it is obvious that cyanosis alone does not permit of differentiation between the venous shunt and the nonvenous shunt type of lesion. Periodic cyanosis, however, is considerably more common with the former (26 per cent) than with the latter (15 per cent).

Among the sixty-two patients were eight (13 per cent, approximately) who presented a syndrome that was almost totally absent in the smaller group of twenty. The syndrome usually consisted of the appearance of cyanosis in association with respiratory distress (hyperpnea or apnea) and with muscular and nervous disturbances of some sort. Varying combinations of signs and symptoms occurred (table 1). In one patient the cyanosis was absent (case 7), but in the other seven there was either a transient cyanosis during the attacks or a constant cyanosis that became much more pronounced during the seizures. It may be observed that only one patient (case 2) had patency of the ductus as the sole defect that could account for the disturbance. In each of three others (cases 1, 4 and 6) there was an accompanying patent foramen ovale or a defect in the interventricular septum. In the remainder (cases 3, 5, 7 and 8), it can be seen that symptoms must necessarily be accounted for by a lesion other than patent ductus arteriosus. Thus it appears that this syndrome is not typical of a specific lesion, but may be an accompaniment of any defect that gives rise to a venous shunt. Similar disturbances occurred in one child who had transposition of the aorta and pulmonary artery without other defects in the heart. Among several other patients with trans-

position of the great vessels, as well as among a number with complete absence of one or more of the cardiac septums, no such symptoms appeared.

An additional group of five (table 2) from among the sixty-two patients presented periodic convulsion-like seizures without cyanosis or

TABLE 1.—*Incidence of Venous Shunt Syndrome Among Sixty-Two Patients*

No.	Age	Type of Disturbance	Lesion
1	6 wks.	Periodic flaccidity with drowsiness and cyanosis	Patent ductus arteriosus; patent foramen ovale; cardiac hypertrophy
2	5½ mos.	Convulsive seizures with cyanosis	Patent ductus arteriosus
3	13 mos.	Daily attacks of respiratory distress with cyanosis of a few minutes to one hour's duration, followed by sleep	Defect in interventricular septum; patent foramen ovale; transposition of aorta; cardiac hypertrophy
4	1 yr.	Convulsion-like seizures with cyanosis, after eighth month of life	Defect in interventricular septum; patent ductus arteriosus; coarctation of descending aorta; cardiac hypertrophy
5	2 yrs.	Convulsion-like seizures with cyanosis followed by drowsiness	Defect in interventricular septum; transposition of aorta; pulmonic stenosis; hypertrophy of right ventricle (tetralogy of Fallot); red cell count: 7,500,000
6	5 wks.	Attacks of apnea with slight cyanosis and a slow heart rate accompanied by flaccidity of the entire body	Patent ductus arteriosus; patent foramen ovale
7	2 wks.	Convulsive seizures with respiratory distress	Defect in interventricular septum; transposition of great vessels
8	6 days	Attacks of apnea with deep cyanosis, with a fall in pulse rate to about 40, of two or three minutes' duration	Defect in interventricular septum; stenosis of pulmonary valve; cardiac hypertrophy and dilatation, especially of the right side of the heart

TABLE 2.—*Modified Venous Shunt Syndrome*

No.	Age	Type of Disturbance	Lesion
1	5 wks.	Periodic convulsive seizures	Patent ductus arteriosus; patent foramen ovale; hypertrophy of right ventricle
2	4 wks.	Slight semiconvulsive seizures	Patent ductus arteriosus
3	2 mos.	Convulsive seizures beginning at age of 2 weeks	Patent ductus arteriosus
4	3½ mos.	Slight convulsive seizures daily	Patent ductus arteriosus; thickening of all the valves; cardiac hypertrophy and dilatation
5	17 yrs.	Convulsive seizures during childhood	Pulmonary stenosis; patent interventricular septum

a marked respiratory distress. Such seizures were absent among the twenty patients with the nonvenous shunt type of lesions.

Consideration of the mechanism responsible for the appearance and nonappearance of cyanosis and other signs brings to mind the fact that under normal conditions an abnormal communication between the right and the left side of the heart does not produce a venous shunt. On the contrary, since the pressure is greater in the arterial side, any shunt will be in the nature of an arterial flow to the venous side. Thus

there is an adequate explanation of the absence of signs and symptoms in many patients who have these defects. When the pressure within the right side of the heart becomes sufficiently elevated, a reversal of flow takes place with the appearance of venous blood in the systemic circulation and with the production of visible cyanosis if the venous shunt is great enough in volume. Apparently, sudden changes in the pressure relationship between the right and the left side of the heart do take place in patients with congenital heart disease, especially when there is a combination of defects in the heart. The venous shunt syndrome in a number of the patients seemed to be induced by the exertion of feeding, and particularly by crying. It is obvious that the venous shunting may be continuous or intermittent or a terminal event depending on the severity and degree of permanence of the conditions altering the dynamics of the circulation. The convulsions with cyanosis are accounted for by reason of the anoxemia induced by the venous shunt. That all patients with defects that actually do give rise to venous shunts are not subject to such symptoms may be due to adaptation to the oxygen deficiency and in part to the development of polycythemia, but it is due usually, in all likelihood, to the small volume of the shunt. It is difficult to explain the attacks of convulsion without cyanosis, since it is unlikely that a venous shunt in the heart could produce a local anoxemia of the brain sufficient to give rise to convulsions without also producing cyanosis. Yet five patients with lesions of the heart of the venous shunt variety did have convulsive seizures, with no other adequate cause revealed at autopsy in most of them. It is true that four of the thirteen patients listed in the two tables did have pneumonia, which may have caused the syndrome either primarily or by reason of a sufficient elevation of pressure in the right side of the heart to bring about a venous shunt. Two of these four, however, had the syndrome in the absence of pneumonia.

Five of the thirteen tabulated patients died suddenly. Four of these had patent ductus arteriosus as the sole or chief defect, which emphasizes the contention that this lesion constitutes a pathologic state of importance from the point of view of function, if not of anatomy. Even when uncomplicated by other defects, this lesion must produce a constant strain on the pulmonary circulation and the entire heart owing to the normally existent flow from the aorta to the pulmonary artery through the ductus.

Smith,[1] of London, has called attention to the apparent association of transient cyanosis and apneic attacks with patency of the ductus arteriosus. He reported this lesion in each of a pair of twins in whom

1. Smith, K. S.: Congenital Cardiac Disease in Identical Twins, Arch. Dis. Childhood **4**:330 (Oct.) 1929.

there was transient cyanosis, especially during coughing and crying. During the cyanotic periods, there was a disturbance of respiration, apnea in one infant, hyperpnea in the other. At autopsy, evidences of bronchitis and bronchopneumonia were found, but the sole cardiac defect was patency of the ductus arteriosus. Descriptions are quoted of three cases in which spontaneous attacks of apnea with cyanosis were observed at various intervals, death occurring as the immediate consequence of a severe or prolonged attack, with patency of the ductus arteriosus constituting the sole abnormality found at autopsy. In a 4 weeks old baby whose constant cyanosis varied considerably in depth, the autopsy revealed a ductus arteriosus of about a fourth of the bore of the pulmonary artery. There also was bronchopneumonia of the lower lobes of the lungs. In none of the six patients were there abnormal heart signs, such as enlargement or murmur.

Smith discussed the mode of production of cyanosis in these patients and suggested that the cause lies in a change in blood supply to the lungs brought about by a reversal of the direction of blood flow through the patent ductus arteriosus. He stated that when blood is deflected from the pulmonary circuit through an abnormal passage into the systemic circulation, progressively increasing cyanosis must follow. This is not necessarily true, however, since it has been pointed out by several investigators that the point to which oxygen unsaturation must be raised before cyanosis appears to the eye (cyanotic threshold) cannot be reached by a venous shunt alone until the volume of the shunt equals one third of the total blood flow. It must also be remembered that reduction of the amount of oxidizable hemoglobin in the blood to a sufficiently low level, as in severe anemia, renders cyanosis practically impossible. On the other hand, the venosity of a shunt may be increased by a diminished pulmonary oxygenation and by an increased deoxygenation at the periphery, and probably also by exercise. No explanation of the cause of such a reversal of flow is offered by Smith, other than increased resistance in the pulmonary circuit due to muscular effort on the part of the child, such as crying or coughing, or to pulmonary infection. He expressed the belief that the termination of the attacks of cyanosis may be due to the rise of arterial blood pressure that accompanies asphyxia. The absence of a cardiac murmur in these patients, contrasted with the characteristic murmur in adults with similar lesions, he thought might be due to differences in the size and shape of the ductus. The evidence presented in the present paper seems to show that the symptoms reported by Smith are not typical of patent ductus arteriosus, but may be produced by any defect that gives rise to a venous shunt.

SUMMARY

The clinical records of sixty-two patients with congenital heart lesions, revealed at autopsy, of such a nature as to permit venous shunting were studied in an attempt to determine the presence or absence of characteristic symptoms and signs. Nearly half of these patients presented no clinical abnormalities referable to the circulatory apparatus. While the incidence of cyanosis, periodic as well as constant, was found to be somewhat higher in this group than among twenty other patients whose autopsies revealed congenital defects of the heart that did not permit venous shunting, this sign was found not to differentiate sufficiently the two general types of lesions. Eight (13 per cent, approximately) of the large group presented a syndrome that was almost totally absent in the smaller group with the nonvenous shunt type of defect. In the larger group, five additional patients presented convulsive seizures not accompanied by cyanosis and respiratory distress.

In conclusion, it may be said that when other causes, such as pneumonia, epilepsy, meningitis and severely toxic conditions, can be ruled out and when the patient is known to have congenital heart disease, the occurrence of convulsion-like seizures, often epileptiform in character, sometimes followed by drowsiness and frequently accompanied by hyperpnea, may justly be interpreted as an indication of a lesion, or a combination of lesions, that permits venous shunting, especially if the patient shows a constant cyanosis, no matter how slight, or if the attack is accompanied by a deep cyanosis.

THE ACID-BASE METABOLISM OF A NORMAL CHILD ON DIETS THAT INCREASE IN FAT CONTENT

CHARLES A. WEYMULLER, M.D.
AND
SARAH RATNER, M.A.
BROOKLYN

The very few reported studies of normal children who received ketogenic diets have not included complete data for the acid-base metabolism. In fact, the study of two normal children by Sawyer, Baumann and Stevens,[1] in 1918, furnishes all of the information available for comparison. Yet these reports are lacking in data concerning blood changes, notably those in the inorganic acids and bases.

We have attempted to supply additional material by this investigation of the acid-base metabolism of a normal boy of 9 years who received ketogenic diets.

His medical history and physical examination revealed no reason for excluding him as a subject for this study. Particular investigation was made for any history of recurrent attacks of ketosis or recent infections. None was found.

During the study period the child was under the constant care of two special nurses, one of whom weighed and prepared his food according to a uniform procedure. He was permitted to spend two hours a day quietly in a wheel-chair, and the rest of the day he remained quietly in bed.

Three diets were used for four days each. They had ratios of ketogenic to antiketogenic substances of 1:2, 1.5:1 and 2.6 1. Milk, eggs, rice, salt-free butter, cream, Lister muffins and sucrose were used in varying proportions. The food was distributed daily over four meals and each meal had the same ratio as the whole diet (table 1).

The basal caloric requirement indicated by the Benedict and Talbot tables [2] was increased by 30 per cent. It was maintained at this level. All diets were neutral with respect to the acid and base radicals of the

Submitted for publication, July 18, 1931.
From the Department of Pediatrics of the Long Island College Hospital.

1. Sawyer, L.; Baumann, L., and Stevens, F.: Studies of Acid Production: II. The Mineral Loss During Acidosis, J. Biol. Chem. **33**:103, 1918.

2. Benedict, F. G., and Talbot, F. B.: Metabolism and Growth from Birth to Puberty, pub. no. 302, Carnegie Inst., Washington, 1921.

ash. Furthermore, the amounts of the individual acid radicals and the base radicals were constant for all three diets.

We thought that a neutral diet would permit the observation of acid-base metabolism uninfluenced by the necessity of having to take care of excess acid or base from the food. Moreover, since all three diets were neutral, the developing acidosis due to ketosis should presumably have been the only variable factor.

The inorganic constituents of the food were calculated in terms of cubic centimeters of tenth-normal solution from the Sherman tables.[3] Phosphorus was given the physiologic valence of 1.8.[4] The chloride content of the food was determined in the laboratory and enough added to make the chloride intake sufficient for body needs and constant throughout. The water intake, including that contained in the food, was fixed at 1,975 cc. and maintained for the entire experimental period.

TABLE 1.—*Daily Content of Each Diet Ingested*

Ketogenic : antiketogenic ratio	1 : 2	1.5 : 1	2.6 : 1
Protein, Gm.	59	64	70
Fat, Gm.	60	106	117
Carbohydrate, Gm.	120	38	1
Total calories	1,293	1,403	1,382
Water, cc.	1,977	1,963	1,975
Phosphorus, cc. N/10*	671	686	710
Chloride, cc. N/10	599	583	601
Sulphur, cc. N/10	377	369	359
Total inorganic acids, cc. N/10	1,647	1,638	1,670
Total fixed base, cc. N/10	1,615	1,609	1,626

* Valence 1.8.

The patient was weighed three times a day under uniform conditions, that is, before eating and after voiding. The specimens of urine for each twenty-four hours were preserved with toluene and chloroform. Determinations of p_H, ammonia, titratable acidity and organic acids were performed the day of the collections. Forty-eight hour collections of feces were made and separated with carmine administered on the morning of the first and third day of each period. These specimens were kept on ice in closed containers and preserved with thymol. Blood was collected from the arm vein, without stasis, on the fourth day of each period. Blood serum measurements were made of total base,[5] total carbon dioxide content,[6] p_H,[7]

3. Sherman, H. C.: Chemistry of Food and Nutrition, New York, The Macmillan Company, 1926, appendix B, table 11.

4. Gamble, J. L.; Ross, G. S., and Tisdall, F. F.: The Metabolism of Fixed Base During Fasting, J. Biol. Chem. **57**:633, 1923.

5. Stadie, W. C., and Ross, F. W.: A Micro Method for the Determination of Base in Blood and Serum and Other Biological Materials, J. Biol. Chem. **65**: 735, 1925.

6. Van Slyke, D. D., and Neill, J. M.: The Determination of Gases in Blood and Other Solutions by Vacuum Extraction and Manometric Measurement, J. Biol. Chem. **61**:523, 1924.

7. Hastings, A. B., and Sendroy, J.: Studies of Acidosis: XX. The Colorimetric Determination of Blood PH at Body Temperature Without Buffer Standards, J. Biol. Chem. **61**:695, 1924.

protein,[8] chlorides,[9] phosphates,[10] acetone bodies [11] and whole blood sugar.[12] In the urine, p_H,[13] organic acids,[14] titratable acidity,[15] acetone bodies,[16] ammonia,[17] total base,[5] chlorides,[18] phosphates,[19] sulphates [20] and creatinine [21] were determined. In the feces [22] total base,[5] phosphates [19] and chlorides [9] were determined.

In short, the neutral diets of constant acid, base, caloric and fluid contents were altered only as regards the ketogenic-antiketogenic ratio.

RESULTS

The results for the blood (table 2) were as follows: The bicarbonate decreased from 61.1 to 45 per cent by volume. The p_H changed from 7.42 to 7.32, and ketone bodies were present in the blood

8. Neuhausen, B. S., and Rioch, D. M.: The Refractometric Determination of Serum Proteins, J. Biol. Chem. **55**:353, 1923.

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13. Hastings, A. B.; Sendroy, J., and Robson, W.: Studies of Acidosis: XXI. The Colorimetric Determination of the PH of Urine, J. Biol. Chem. **65**:381, 1925.

14. Van Slyke, D. D., and Palmer, W. W.: Studies of Acidosis: XVI. Titration of Organic Acid in Urine, J. Biol. Chem. **41**:567, 1920.

15. Henderson, L. J.: A Critical Study of the Process of Acid Excretion, J. Biol. Chem. **9**:403, 1911.

16. Van Slyke, D. D.: Studies of Acidosis: VII. The Determination of Beta-Hydroxybutyric Acid, Aceto-Acetic Acid and Acetone in Urine, J. Biol. Chem. **32**:455, 1917.

17. Folin, O., and Macallum, A. B.: On the Determination of Ammonia in Urine, J. Biol. Chem. **11**:523, 1912.

18. Harvey, S. C.: The Quantitative Determination of the Chlorids in the Urine, Arch. Int. Med. **6**:12 (July) 1910.

19. Fiske, C. H., and Subbarow, Y.: The Colorimetric Determination of Phosphorous, J. Biol. Chem. **66**:375, 1925.

20. Folin, O.: On Sulphate and Sulphur Determination, J. Biol. Chem. **1**:131, 1905.

21. Folin, O.: On the Determination of Creatinine and Creatine in Urine, J. Biol. Chem. **17**:469, 1914.

22. The feces were triturated to a fine suspension with distilled water and weighed aliquots taken for analysis. Each aliquot was wet ashed with sulphuric and nitric acids and made up to a definite volume. Aliquots of the digestate were then used for the determination of total base and phosphorus. Chlorides were determined directly on the original suspension.

to the extent of 5.7 cc. tenth-normal betahydroxybutyric acid on the most ketogenic diet. The total base concentration of the blood remained constant in spite of the increased demands. The chlorides rose from 596 to 618 mg. of sodium chloride. There was no appreciable change in the phosphates.

These results are similar for the most part to the changes found by Gamble [4] in the serum of children who developed ketosis due to fasting. We, however, noted a rise in serum chlorides at the time Gamble found a decrease. Coincident therewith he noted a minimal excretion of chlorides in the urine. We found a definite increase in urinary chlorides when the serum value rose despite constant intake. It seems probable that fasting accounted for the conservation of chlorides by Gamble's patient, while no such necessity existed for our patient.

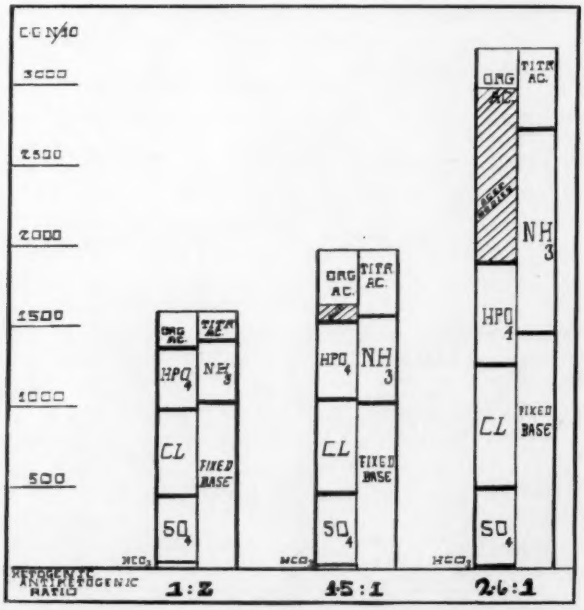
TABLE 2.—*Acid-Base Composition of Blood Serum*

	Ketogenic : Antiketogenic Ratio					
	1 : 2		1.5 : 1		2.6 : 1	
	Mg. per 100 Cc.	Cc. N/10 per 100 Cc.	Mg. per 100 Cc.	Cc. N/10 per 100 Cc.	Mg. per 100 Cc.	Cc. N/10 per 100 Cc.
Bicarbonate, per cent by volume	61.1	26.0	54.8	23.2	45.0	18.9
Protein, Gm.	7.72	18.8	7.63	18.3	7.83	18.2
Chlorides (NaCl)	596	102.1	596	102.1	618	105.6
Phosphates	4.4	2.6	4.3	2.5	4	2.3
Ketone bodies	....	....	....	....	33.3	5.7
Total acids		149.5		146.1		150.7
Total base		152.0		151.4		153.8
Residual acids		2.5		5.3		3.1
ps.	7.42		7.38		7.32	
Dextrose	80.3		70.2		65.6	

That a ketone acidosis was produced was further confirmed by the urinary determinations. Separate estimations of organic acids and of total acetone bodies as betahydroxybutyric acid show that at the height of the acidosis 82 per cent of the organic acids were excreted in the form of ketone bodies (chart). The presence in the urine of other substances also shows the extent of the acidosis. The maximum organic acid excretion was six times the value found on the first diet; titratable acidity three times, and ammonia three times. These measurements are graphically portrayed in the chart, and although no new facts appear, they are excellently descriptive of the process of acid excretion in the urine.

Less is known, however, of the excretion of fixed base and inorganic acids. Before considering the intake and excretion of these sub-

stances individually, the data are presented in table 3 to show the amounts per twenty-four hours of all the acids and bases excreted by way of the kidneys. Following the method of Gamble,[4] the values for titratable acidity and ammonia were subtracted from the sum of the acid radicals. The hydrogen carbonate (HCO_3^-) values included with the latter were calculated from the p_H with the aid of Gamble's data.[23] All the other constituents were directly determined. The results of the foregoing subtractions represent the total base present as determined by difference. These figures were compared with the values obtained by



Graphic presentation of the acid-base composition of the urine (average of last forty-eight hours of each period).

direct determination. The agreement was satisfactory for results of this nature when the calculated value, containing the cumulative errors of seven determinations, was compared with the direct result of a single method. The average difference was 5 per cent of the direct determination.

In any consideration of the effects of dietary changes on the excretion, endogenous sources must also be included. Our patient was in nitrogen equilibrium only on the first diet. On the second and third

23. Gamble, J. L.: Carbonic Acid and Bicarbonate in Urine, J. Biol. Chem. **51**:295, 1922.

diets, body tissue was catabolized. The concentrations of the inorganic constituents of this tissue, which were also excreted, were calculated from the negative nitrogen balance using Katz'[24] figures for human muscle tissue. The values were subtracted from the excretions in each instance.

It may readily be seen (table 4) that during the eight days when ketosis was developing there was an increase in the total excretion of

TABLE 3.—*Total Acid and Base Excreted in the Urine as Cubic Centimeters Tenth Normal per Twenty-Four Hours; Average of Last Two Days of Each Period*

Ketogenic : antiketogenic ratio	1 : 2	1.5 : 1	2.6 : 1
Organic acids	214	313	1,320
Phosphates*	389	491	637
Chlorides	537	567	745
Sulphates	407	474	508
Bicarbonate	44	11	10
Total acids	1,591	1,856	3,220
Titratable acid	160	290	488
	1,431	1,566	2,732
Ammonia	392	536	1,258
Fixed base by difference	1,039	1,030	1,474
Fixed base, direct determination	1,004	981	1,389

* Valence 1.8.

TABLE 4.—*Excretion of Fixed Base and Inorganic Acid as Cubic Centimeters Tenth Normal Per Twenty-Four Hours; Average of Last Two Days of Each Period*

	Fixed Base			Inorganic Acid		
Ketogenic : antiketogenic ratio	1 : 2	1.5 : 1	2.6 : 1	1 : 2	1.5 : 1	2.6 : 1
Urine	1,004	981	1,389	1,334	1,532	1,890
Feces	274	421	157	252	321	109
Total excretion	1,278	1,402	1,546	1,586	1,853	1,999
Endogenous	0	23	43	0	45	83
Excretion (exogenous)	1,278	1,379	1,503	1,586	1,808	1,916
Increase over first period	0	101	225	0	218	330

fixed base and fixed acid. The fixed base excretion as cubic centimeters tenth normal during the foreperiod was 1,278, which increased to 1,379 with a diet of K 1.5 : AK 1 and finally to 1,503 on the diet K 2.6 : AK 1. The total acid excretion as cubic centimeters tenth normal was 1,586 with diet K 1 : AK 2 and increased to 1,808 on K 1.5 : AK 1 and finally

24. Katz, J.: Die mineralischen Bestandteile des Meskelfleisches, Arch. f. d. ges. Physiol. **63**:18, 1896.

to 1,916 on K 2.6 : AK 1. Because of the errors involved in using average values from tables, we have made no attempt to calculate absolute balances of the inorganic constituents. We have, however, accepted these tables as sufficiently reliable to assume that the intake was fairly constant, so that the variations in excretion can reasonably be compared.

It is interesting to note that while this increase in total excretion of acid and base occurred, there was practically no change in the ratio of excretion of these substances. During the foreperiod, when diet K 1 : AK 2 was ingested, the acid-base ratio was 1.00 : 0.81; it became 1.00 : 0.75 with diet K 1.5 : AK 1 and 1.00 : 0.78 with diet K 2.6 : AK 1. This strongly suggests that the original diet, although calculated from the foods taken as having an acid-base ratio of 1.00 : 1.00, actually had a ratio of 1.00 : 0.8.

The most likely explanation of the increase in total excretion is that there was a loss of body fluid just as occurs in ketosis due to fasting.

TABLE 5.—*Record of Daily Changes in Urine, Creatinine and Nitrogen Excretion: Nitrogen Balance and Weight*

Ratio	Date	Urine, Cc.	Creatinine, Mg.	Nitrogen Excretion, Gm.	Nitrogen Balance, Gm.	Body Weight, Kg.
K 1 : AK 2	4/ 9/29	1,705	500	8.82	+0.59	26.226
	4/10/29	1,280	500	8.99	+0.42	26.079
	4/11/29	1,400	500	8.60	+0.81	25.947
	4/12/29	1,307	502	8.93	+0.48	25.966
K 1.5 : AK 1	4/13/29	1,295	504	10.66	−0.49	26.032
	4/14/29	1,530	476	11.14	−0.97	25,853
	4/15/29	1,570	481	10.94	−0.77	25.540
	4/16/29	1,130	464	10.54	−0.37	25.805
K 2.6 : AK 1	4/17/29	1,240	461	14.55	−3.43	25.654
	4/18/29	1,570	445	13.37	−2.25	25.502
	4/19/29	1,230	468	13.23	−2.11	25.379
	4/20/29	1,195	395	10.30	+0.82	25.366

TABLE 6.—*Individual Inorganic Acid Excretion as Cubic Centimeters Tenth Normal Per Twenty-Four Hours; Average of Last Two Days of Each Period*

	Phosphates*			Chlorides			Sulphates		
Ketogenic : antiketogenic ratio	1:2	1.5:1	2.6:1	1:2	1.5:1	2.6:1	1:2	1.5:1	2.6:1
Urine	389	491	637	537	567	745	407	474	508
Feces	252	321	109	3	7	2	...	...	...
Total excretion	641	812	746	540	574	747	407	474	508
Endogenous	0	20	37	0	3	6	0	22	40
Excretion (exogenous)	641	792	709	540	571	741	407	452	468
Increase over first period	0	151	68	0	31	201	0	45	61

* Valence 1.8.

There was a steady loss of weight from 26.226 Kg. on the first day to 25.226 Kg. on the twelfth day. The loss due to tissue destruction (table 5) as calculated from the negative nitrogen balance amounted to 217 Gm. Any expected diuresis predicted from the weight loss not due to tissue destruction would give a figure of much the same magnitude as the error caused by omission of insensible perspiration from the calculations.

We will consider next the excretion of individual inorganic acid constituents. The phosphate excretion (table 6) rose from 641 cubic centimeters tenth normal during the foreperiod to 792 during period 2 and 709 during period 3. The chloride excretion rose from 540 during period 1 to 571 during period 2 and 741 during period 3. The sulphate rose from 407 during period 1 to 452 during period 2 and 468 during period 3.

The interesting finding that the increase in acid excretion during the second period was chiefly composed of monohydrogen phosphate ($HPO_4^=$) and of chloride during the third seems best explained by the surmise that the loss of body fluid during the second period is largely from the intracellular compartment where monohydrogen phosphate ($HPO_4^=$) is the chief acid radical, and that this is followed during the third period by a loss of extracellular water as indicated by the increase in chloride excretion. Naturally, such an interpretation requires the acceptance of Gamble's [4] concept of the mechanism of body fluid exchange during acidosis. In support of our surmise, it might be mentioned that the reduction of the level of dextrose metabolism (blood sugar, 80.3; 70.2; 65.6) might possibly have something to do with the release of monohydrogen phosphate ($HPO_4^=$), according to the recent evidences of relationship of inorganic phosphate to sugar metabolism.

Although we noted an increase in sulphate excretion from 407 cubic centimeters tenth normal in period 1 to 452 in period 2 and 468 in period 3, no reasonable explanation occurs to us.

We feel that this study fairly depicts the changes that occurred, because it covered the considerable period of twelve days and was subdivided so that the patient was permitted four days to become adjusted to each diet change. Furthermore, only an average of the measurements of the last two days of each period was accepted as representative of the patient's reaction to the given diet. Even though the errors due to calculation of food values from tables made it necessary to compare excretion values instead of absolute balances, the adjustments that occurred are clearly discernible; while the events that occur during the ketosis of fasting are well known, there have been no adequate studies of the adjustments which accompany the ketosis induced while intake is adequate.

We realize that what we describe, if it happens with regularity, represents adjustments made during the transition from an ordinary diet to a ketogenic diet in which the chief event is probably a reduction of the volume of body fluids to a lower level. When this level is reached the usual relationship of acid base intake to excretion is probably approximated. At any rate, our findings do not justify the inference that this ketogenic regimen causes a very great depletion of inorganic substances.

96 Joralemon Street.

INFANTILE DIARRHEA

PRELIMINARY REPORT

MARSH W. POOLE, M.D.
AND
THOMAS B. COOLEY, M.D.
WITH THE TECHNICAL ASSISTANCE OF MISS LUCIA ELLWART
DETROIT

In Detroit the most severe and rapidly fatal forms of infantile diarrhea begin to make their appearance about the third week of August, reach a peak during September and become less frequent in early October. This curve corresponds closely to that observed in other cities having approximately the same climatic conditions. Despite the unusual and excessive heat of the early summer of 1930, comparatively few patients with diarrhea were admitted to the Children's Hospital until the last week of August; hence our studies have all been made over a rather brief period of about five weeks.

During the time that we have been conducting our observations, there have been admitted to our ward patients suffering from diarrheas of all degrees of severity and of various etiology. We have experienced considerable difficulty in classification, because often it was practically impossible to make a definite statement as to the cause which, in any given instance, had operated to initiate and keep the diarrhea active until we received the patient, which usually was at least several days after the onset. In a great majority of cases, the condition had progressed sufficiently far for the child to show signs of dehydration and toxemia, while many patients were admitted in coma or semistupor.

Observations were made on the blood at admission; whenever possible, this was done before any form of therapy had been instituted. Such observations were repeated at intervals during the children's stay in the hospital to check the results of treatment or to determine, if possible, the reasons for their failure to improve clinically. We have been particularly interested in patients showing the most severe symptoms in an endeavor to rationalize, if possible, the treatment instituted, as we have felt that our previous efforts were at best rather haphazard and sometimes probably misdirected.

During previous years, blood typing was done immediately for all patients admitted to the Children's Hospital with diarrhea so that a

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suitable donor would be available for transfusion at short notice. Whenever the patient's condition seemed to warrant it, transfusion was done as soon as possible after admission; otherwise, fluids were given subcutaneously or intravenously followed by transfusion whenever that procedure seemed indicated by a progression of the patient's symptoms or if a relapse occurred after several days of apparently good progress. In the beginning of the present series this plan was continued according to our usual routine until we had accumulated sufficient data to convince us that this plan was not applicable to all cases and even harmful in some instances, as will be shown in individual case histories.

In considering the changes that occurred in dehydration (anhydremia) in infants, Marriott [1] found that when the blood showed increased viscosity, increased nonprotein nitrogen (due to retention and accelerated destruction of protein), decreased oxygen-carrying capacity and decreased volume and flow, there were impaired renal function, negative nitrogen balance, fever and increased destruction of body protein. Haden and Orr,[2] working experimentally on dogs, produced dehydration by the injection of a 50 per cent sucrose solution, and demonstrated the following facts: 1. Four of five of their animals showed a terminal rise in nonprotein nitrogen and urea nitrogen. 2. Blood chlorides were uniformly elevated (average of 13.9 per cent). 3. The fibrinogen content was doubled in all cases. 4. The total protein of the serum (largely albumin) showed an average increase of 18 per cent. 5. The plasma percentage, as shown by the hematocrit tube, was decreased in all (in three there was a terminal increase).

Other observers have studied the chemistry in new-born infants suffering from inanition fever and have used various methods for estimating the blood concentration, notably Sherman, Pucher and Lohnes,[3] who made their calculations by drying a weighed sample of oxalated blood at a temperature of from 75 to 80 degrees. Bakwin [4] and Bakwin and Rivkin [5] determined the concentration of serum proteins by the refractometer, and used this as an index of the degree of blood concentration. Schloss, however, has cautioned against drawing conclusions from the estimation of the serum or plasma proteins, and

1. Marriott, W. McK.: Physiol. Rev. **44**:275, 1923.

2. Haden, R. L., and Orr, T. G.: J. Exper. Med. **49**:945 (June) 1929.

3. Sherman, D. H.; Pucher, G. W., and Lohnes, H. R.: Blood Chemistry in the New-Born, Am. J. Dis. Child. **30**:496 (Oct.) 1925.

4. Bakwin, H.: The Effect of Fluid on the Temperature and Blood Concentration in the New-Born with Fever, Am. J. Dis. Child. **27**:578 (June) 1924.

5. Bakwin, H., and Rivkin, H.: The Estimation of the Volume of Blood in Normal Infants and in Infants with Severe Malnutrition, Am. J. Dis. Child. **27**:340 (April) 1924.

McIntosh [6] in studying the blood of dehydrated infants, pointed out that the behavior of plasma protein was not uniform.

To estimate the total volume of blood by the carbon dioxide method of Haldane and Smith [7] or by the dye method of Keith, Rowntree and Geraghty [8] seemed to offer technical difficulties that more than outweighed their obvious advantages in the type of acutely ill patient with which we were dealing, so that no observations were made by either of these methods. We also considered making observations on the surface tension of the blood, but after noting that Clark, Nicholls [9] and Haden and Orr [10] had found little variation, except in case of lipemia, there appeared to be little use of following that particular subject any further.

Viscosity of the blood has received considerable attention from numerous authors, namely, Haden and Orr,[11] Lecomte du Noüy,[12] Chevallier,[13] Mikulowski and Chmielewska [14] and others, because of its importance in the rate of blood flow and hence its relation to the oxygen-carbon dioxide exchange as well as to the excretion of the products of metabolism. We have not made studies of viscosity because of the impracticability of making too many examinations of the blood of these acutely ill patients, and chiefly because we felt that other methods would yield observations of more practical value.

After consideration of the previously enumerated facts, we made the following estimations for each patient whenever possible: (1) hemoglobin (Sahli), (2) red cell count, (3) white cell count, (4) plasma-cell ratio (hematocrit tube), (5) specific gravity of the blood serum and (6) total chlorides. The reasons for this choice were that by estimating the specific gravity of the blood serum we felt that we should have an accurate index of the concentration of both electrolytes and proteins, while the plasma-cell ratio was an easily determined indication of the degree of loss of water from the blood plasma, which was further checked by the hemoglobin estimation and the red cell count.

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6. McIntosh, R.; Kajdi, L., and Meeker, D.: J. Clin. Investigation **9**:333 (Oct.) 1930; Blood Volume Studies in Dehydration, Am. J. Dis. Child. **39**:1345 (June) 1930.
7. Haldane and Smith: J. Physiol. **25**:331, 1900.
8. Keith, N. M.; Rowntree, L. G., and Geraghty, J. T.: A Method for the Determination of Plasma and Blood Volume, Arch. Int. Med. **16**:547 (Oct.) 1915.
9. Nicholls, E. G.: Bull. Johns Hopkins Hosp. **42**:358 (June) 1928.
10. Haden and Orr: J. Exper. Med. **44**:425, 1926.
11. Haden and Orr: J. Exper. Med. **44**:419, 1926.
12. du Noüy, P. L.: Compt. rend. Acad. d. sc. **186**:804 (March) 1928.
13. Chevallier, A.: J. de méd. de Lyon **9**:235 (April) 1928.
14. Mikulowski and Chmielewska: Acta pædiat. **8**:185, 1928.

The total chlorides were studied because it has been abundantly shown by Marriott, Hartman,[15] Schoenthal[16] and Hamilton, Kajdi and Meeker,[17] in their work on dehydrated patients, as well as experimentally by Haden and Orr,[2] that the acidosis in such patients is largely chloride acidosis, so that taken in conjunction with the clinical picture of any child, we considered it helpful as a guide for proper therapy. Samples of blood for chloride estimations as well as those for phosphorus, sugar and calcium were taken from the femoral or external jugular veins, while the figures for specific gravity, hemoglobin and red cell count are based on samples taken by deep puncture of the heel.

Our serum-specific gravity readings were made by the Hammerschlag method after the samples were centrifugated in carefully corked tubes. Barlow and Whitehead,[18] using pigeons' blood, after checking

TABLE 1.—*Serologic Findings and Hematocrit Readings in Patients with Conditions Other Than Diarrhea*

Patient	Age, Mo.	Diagnosis	Hemoglobin, Mg.	Red Cells	Serum Specific Gravity	Hematocrit	
						Cells, per Cent	Plasma, per Cent
Comstock	4	Nasopharyngitis	81	4,800,000	1.028	32.0	68.0
Porter	8	Otitis media	70	4,040,000	1.029	32.8	67.2
Murphy	5	Feeding disorder	75	4,240,000	1.027	29.3	70.7
Jackson	13	Postoperative mastoiditis	77	4,380,000	1.027	24.4	75.6
Benson	1	Circum.	74	4,220,000	1.028	30.7	69.3
DeMarico	2	Fracture	70	4,460,000	1.028	25.6	74.4
Marshall	3	Circum.	78	4,660,000	1.027	24.0	76.0
Schaffer	3½	Atresia ani	79	4,550,000	1.027	22.5	77.5
Frestine	9	Circum.	78	4,600,000	1.028	31.0	69.0
Neal	5	Malnutrition; rickets; otitis media	62	3,860,000	1.027	27.0	73.0
Biggs	10	Malnutrition; feeding disorder	70	4,040,000	1.027	28.0	72.0
Stone	2	Hydrocele	66	4,080,000	1.027	22.0	78.0

this technic for whole blood and serum, adopted it in their experiments on anemia; we have found it suitable for frequent observations and apparently sufficiently accurate for our purposes. Barbour and Hamilton,[19] however, claim even greater accuracy for their falling-drop method, and have pointed out that it, too, may be used for frequent determinations in numerous clinical conditions associated with distur-

15. Hartman, A. F.: Chemical Changes Occurring in the Body as the Result of Certain Diseases, Am. J. Dis. Child. **35**:557 (April) 1928.

16. Schoenthal, L.: Acid-Base Metabolism, Am. J. Dis. Child. **37**:244 (Feb.) 1929.

17. Hamilton, B.; Kajdi, L., and Meeker, D.: The Acidosis of Acute Diarrhea in Infancy, Am. J. Dis. Child. **38**:314 (Aug.) 1929.

18. Barlow, O. W., and Whitehead, R. W.: Am. J. Physiol. **87**:51 (Nov.) 1928.

19. Barbour, H. G., and Hamilton, W. F.: J. Biol. Chem. **69**:625 (Aug.) 1926; Falling Drop Method for Determining Specific Gravity, J. A. M. A. **88**:91 (Jan. 8) 1927.

bance in water balance. Spencer [20] used the latter method, and found it reliable in estimating the specific gravity in dehydrated infants.

Hematocrit readings were made by drawing blood up into small tubes, the walls of which had been previously covered by a fine film of dry oxalate. The tubes were then sealed with collodion and centrifugated at a constant high speed for thirty minutes.

Table 1 shows the figures obtained for a series of infants admitted to the hospital or outpatient department for conditions other than diarrhea; all of them had a temperature of less than 100 F., and care was taken to exclude any patients having a history of vomiting or diarrhea or showing evidences of dehydration. We have assumed that these values represent nearly normal figures for infants of their respec-

TABLE 2.—*Findings in Patients Admitted with Mild or Moderately Severe Cases of Diarrhea*

Patient	Age	Hemoglobin, Mg.	Red Cells	White Cells	Serum Specific Gravity	Hematocrit		Total Chloride, Mg.
						Cells, per Cent	Plasma, per Cent	
Getz	4 mo.	76	4,380,000	6,400	.....	30.0	70.0	...
Blair	8 mo.	72	4,240,000	8,400	.....	....	....	...
Gaffney	5 mo.	55	4,480,000	8,800	1.030	31.0	69.0	680
Tedford	8 mo.	80	5,020,000	9,000	1.028	29.4	70.6	620
Jones	5 mo.	74	4,140,000	5,800	1.029	33.3	66.7	390
Holton	13 mo.	74	4,480,000	8,800	1.027	30.0	70.0	430
Smith	1 mo.	88	5,080,000	18,200	1.030	34.1	65.9	...
Sicard	6 mo.	79	4,300,000	.....	1.028	27.6	72.4	...
Kanazig	7 mo.	60	3,344,000	.....	1.027	27.3	72.7	...
Kanazig (2d admis.)	.....	..	3,670,000	.....	1.031	39.5	60.5	420
Williams	12 mo.	60	3,820,000	.....	1.027	26.6	73.4	...
Baxter*	3 mo.	60	3,640,000	.....	1.028	25.0	75.0	380
Rowan	5 wk.	88	4,860,000	.....	1.029	31.0	69.0	...
Johnson	4 wk.	93	5,240,000	9,800	.....	....	....	...
Cavaness	6 wk.	72	3,600,000	.....	1.030	31.4	68.6	645
Gomez	9 mo.	82	5,440,000	5,600†	(1.029	35.0	65.0)	...
Gumm	10 mo.	84	4,020,000	5,000†	(1.032	29.0	71.0)	...

* Patient died following mastoidectomy. Patient was removed from hospital against advice.

† Readings were taken after the patient had been under treatment.

tive ages. It will be noted from table 1 that the specific gravity of the serums of these children, who were either entirely well or suffering from mild illness not associated with disturbances of water balance, showed a remarkable constancy, ranging in all instances from 1.027 to 1.029, regardless of variations in red cell count, percentage of cells or hemoglobin level. In these children who showed no evidence of infection the percentage of cells in the peripheral circulation ranged from 22 to 30.7, with the red cell count varying from 4,080,000 to 4,600,000. In one instance in which the child was suffering from otitis media of mild degree the percentage of cells was 32.8 with a red count of 4,040,000.

Table 2 shows the findings in those patients who were admitted with mild or moderately severe diarrhea, with or without vomiting,

20. Spencer, H.: The Water Content of Blood Serum, Am. J. Dis. Child. **37**:546 (March) 1929.

and who did not show a marked degree of toxemia or dehydration. It will be seen from these figures that there were only three of these patients whose serum showed a specific gravity of over 1.029, and clinically, these three displayed symptoms severe enough to demand active and energetic treatment, i. e., intravenous transfusion of dextrose or saline, and subcutaneous injection of fluids.

In patient D. G., despite a slight increase in the specific gravity of the serum, with a moderate percentage of cells, there was a definite secondary anemia with increase of blood chlorides; hence we believed that the patient would be benefited by transfusion of whole blood together with the administration of water or dextrose solution rather than saline.

TABLE 3.—*Findings in Patients Showing Advanced Toxemia*

Patient	Age	Hemoglobin, Mg.	Red Cells	White Cells	Serum Specific Gravity	Hematocrit		Total Chloride, Mg.
						Cells, per Cent	Plasma, per Cent	
Battles	1 yr. 8 mo.	91	4,220,000	5,600	.....	....	....	...
Baron	4 mo.	110	6,360,000	.....	1.040	41.6	58.4	...
Martin*	10 mo.	108	6,280,000	.....	1.034	41.0	59.0	600
Dodson	15 mo.	55	4,080,000	.....	1.027	31.0	69.0	260
Grigorian*	5 mo.	96	5,840,000	19,500	1.034	37.0	63.0	490
Buckley*	2 mo.	104	5,600,000	3,800	1.035	43.0	57.0	570
Sage*	8 mo.	82	4,570,000	21,400	1.032	33.0	67.0	...
McKinley	5 mo.	78	4,660,000	6,200	1.033	33.0	67.0	610
Hazard	2 mo.	80	4,360,000	7,800	1.032	34.0	66.0	320
Wardrop	4 mo.	101	5,360,000	15,500	1.037	35.6	65.4	...
Anderson	5 mo.	74	4,120,000	6,200	1.031	27.0	73.0	290
Houston*	8 mo.	88	5,380,000	18,400	1.031	37.2	62.8	580
Prevost*	4 mo.	75	3,240,000	14,900	1.035	36.8	63.2	475
Kirby	5 mo.	95	5,540,000	9,600	1.030	37.0	63.0	...

* Patient died.

Patient C. S. showed a fairly severe loss of water, as evidenced by a high cell-plasma ratio, increased specific gravity of the serum, increased red cell count and hemoglobin levels, and it is probable that the increased white count also could be accounted for by the blood concentration.

The blood picture of patient S. K. on the first admission did not show anything remarkable, except mild secondary anemia, but on the second admission, from the increased specific gravity and the fact that the percentage of cells had risen to nearly 40 (in spite of little difference in the red cell count and hemoglobin) it was seen that more drastic therapy was imperative. In this group of cases there were fourteen recoveries, with only one death.

In table 3 we have listed the cases showing advanced toxemia as evidenced by convulsions, coma or stupor, with, usually, severe vomiting, diarrhea, dehydration and high fever. On admission some of them seemed to be moribund, and many showed unmistakable clinical evidence of acidosis or alkalosis.

All of these patients, with the exception of N. D., showed a specific gravity of the serum of from 1.031 to 1.04, while the percentage of cells varied between 27 and 41.6. In this group, too, the majority showed hemoglobin levels and red cell counts well above the average levels, offering confirmatory evidence of blood concentration with its consequent high cell count. Estimations of blood pressure were also made on many of these patients at the time of admission, a small infant cuff with an ordinary mercury manometer being used. If the pressure

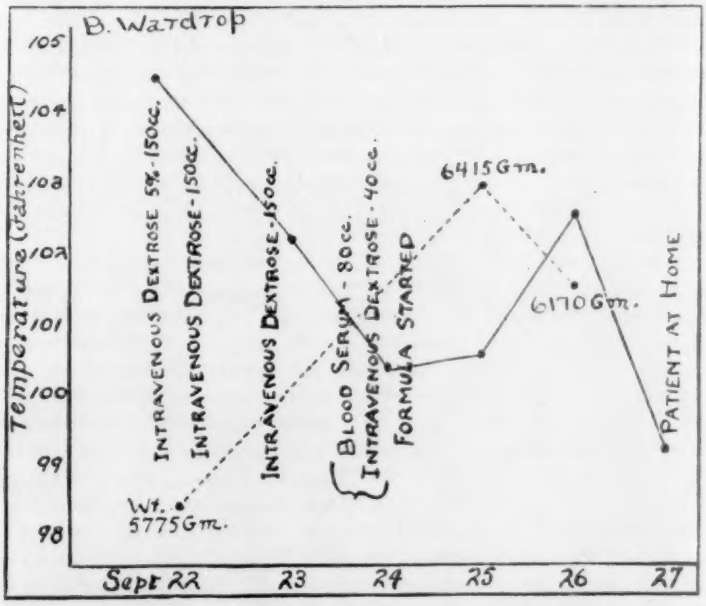

Chart 1.—Course of diarrhea in a girl, aged 4 months, illustrating the value of effecting a rapid return to normal concentration and the effect of the administration of water on the temperature. The solid line represents the temperature and the broken line the weight.

was found to be below the average limits, pitressin was given in full doses.

We feel that in deciding on a plan of treatment in any case these laboratory data should be carefully weighed in conjunction with the clinical picture presented, and that after such consideration a plan of treatment may be selected to which a patient who appears hopeless may often respond beyond every expectation. By repeating the observations at frequent intervals a close check can be kept on progress and response to treatment. This is probably best illustrated by considering individual case histories illustrating the various problems under discussion.

REPORT OF CASES

B. W., a girl, aged 4 months, was admitted to the hospital on Sept. 22, 1930; the parents stated that diarrhea had started seven days previously. At first the stools were slightly green, and as they became more frequent they were copious and watery and contained particles of partly digested food. The mother estimated that there were from fifteen to twenty such movements in the twenty-four hours preceding admission. The vomiting had gradually become worse, until nothing was retained, not even small amounts of water. Sleep had been fitful; the child awoke frequently and emitted a shrill piercing cry. It had also been noted that on the night before admission respiration became rapid and rather labored.

The infant had been breast fed for one month, and was then changed to a condensed milk formula, which had been used until admission to the hospital. Physical examination revealed an acutely ill infant showing moderately severe dehydration, sunken eyes, restlessness and fretfulness. The respirations were forty per minute, and were deep and sighing. The pulse was very rapid. The rest of the examination showed nothing remarkable. The temperature was 104.4 F.; the systolic blood pressure was 90 (taken at the wrist). Laboratory findings were as follows: hemoglobin, 101 mg. per hundred cubic centimeters; red cells, 5,360,000, and white cells, 15,500; specific gravity of the serum, 1.037; percentage of cells, 35.6, and percentage plasma, 64.4.

These findings were interpreted as indicating that the baby had a blood concentration of dangerous degree, and at the same time there was clinical evidence of severe acidosis. Because of the markedly high level of hemoglobin with concentration of red blood cells, transfusion was decided against as being unnecessary and without any indication. Hence the following treatment was carried out: 1. One hundred and fifty cubic centimeters of a 5 per cent solution of dextrose was given intravenously at 4 p. m. and 11 p. m. on September 22, and this dose was repeated at 8 a. m. on September 23. 2. The patient was given sips of a 5 per cent solution of dextrose at frequent intervals, so that she received about 1 ounce (30 cc.) every hour; in each ounce of the solution there was incorporated 3 grains (0.195 Gm.) of sodium bicarbonate. 3. Digalen-Roche and pitressin were administered in full doses. Eighty cubic centimeters of the father's blood serum with 40 cc. of a 5 per cent solution of dextrose was given at 3 p. m., September 23, as the patient still appeared toxic, and, if possible, we wished to raise the immunity against the infections that so often appear in this type of acutely ill patient. A formula of unsweetened evaporated milk, two-thirds strength, with added calcium caseinate and corn syrup was given in 1 ounce quantities, starting on September 24.

On September 25, the patient was discharged, as there was no further vomiting; the signs of dehydration had largely disappeared, the intake of fluids was satisfactory, and an examination of the blood at that time showed: hemoglobin, 66 per cent, and red cells, 3,660,000. The specific gravity of the serum was 1.027. The hematocrit percentage was as follows: cells, 24 per cent; plasma, 76 per cent. The child was kept on an evaporated milk formula at home, the future course being entirely uneventful after a week of carefully increasing the formula both in quantity and in strength.

This patient's chart and history illustrate admirably (1) the effect of rapidly returning the concentration of the blood to normal limits, which was quickly reflected by relief from toxemia, cessation of vomiting and disappearance of signs of severe dehydration; (2) the value of the administration of adequate amounts of sodium bicarbonate in hastening

the relief of acidosis, and (3) the effect of the administration of water on the temperature curve. This point will later be referred to in connection with the discussion of the rôle and incidence of otitis media and other infections in such cases of diarrhea. The fall in temperature is often more striking when adequate amounts of water can be given by mouth rather than saline solution and dextrose by other routes. In this connection it is interesting to note the work of Schloss [21] and Meyer,[22] who found that different substances of equal osmotic concentration when administered in equal amounts did not produce the same types of fever reaction, and that the most marked difference was between the salts of sodium and calcium. We have felt that relief from acidosis is hastened by the administration of sodium bicarbonate while fluids are being pushed to combat the dehydration. Gamble,[23] however, stated that he has found that sodium bicarbonate is occasionally harmful, and that

TABLE 4.—*Showing Danger of Overloading Circulation with Cells by Transfusion*

Dodson, 15 mo.	Hemoglobin, Mg.	Red Cells	Serum Specific Gravity	Hematocrit: Cells, per Cent	Hematocrit: Plasma, per Cent	Gastric p_H
Sept. 8.....	55	4,080,000	1.027	31	69	Sept. 9; 5.4
Sept. 12 Blood transfusion						Sept. 12; 3.0
Sept. 13.....	56	3,880,000	1.036	26.1	73.9	Sept. 17; 3.0
Sept. 15.....	74	5,220,000	1.037	39.3	60.7	Sept. 22; 4.8
Sept. 15 Blood transfusion						
Sept. 17.....	96	6,000,000	1.037	45	55	Sept. 24; 4.8
Sept. 19 Intravenous dextrose solution (5%)						
Sept. 21.....	81	5,280,000	1.030	35.5	64.5	Sept. 25; 4.2
Sept. 29.....	83	5,000,000	1.028	32	68	Oct. 4; 4.2
Oct. 23.....	65	3,190,000	1.028	25.5	74.5	Oct. 6; 4.4

Total chloride: Sept. 8, 200 mg.; Sept. 17, 370 mg.

it is not ordinarily indicated as saline or dextrose is effective. He has further pointed out [24] that the administration of water serves to restore normal renal function, which is impaired in severe dehydration, thus enabling the body to reestablish a proper balance between the acid and the basic salts.

The history of the patient N. D. (table 4) illustrates what occurred in some of our early cases in which no attempt was made to follow other than what previously had been the routine practice of relying almost entirely on repeated transfusions, the indications being based solely on the continuation or progression of symptoms.

On admission the patient was moderately ill; the specific gravity of the serum was within normal limits, as was the percentage of red blood cells. Four days later, because of severe vomiting, loss of weight and elevation of temperature, a

21. Schloss: Biochem. Ztschr. **18**:14, 1909.
22. Meyer: Jahrb. f. Kinderh. **71**:1, 1910.
23. Gamble, J. L.: New England J. Med. **199**:1318 (Dec. 27) 1928.
24. Gamble, J. L.: New England J. Med. **201**:909 (Nov. 7) 1929.

transfusion was performed, which was followed by little, if any, improvement, and twenty-four hours later the specific gravity of the serum had reached 1.036. Three days after the first transfusion, a second one was given. Immediately afterward an extensive erythema of the skin appeared; desquamation of the affected skin took place in the next few days, during which the patient showed little clinical improvement. After this second transfusion the percentage of cells rose to the extremely high point of 45 per cent and the serum specific gravity to 1.037.

In reviewing the chart and progress of this patient we felt that the treatment had been misdirected, and that there had been an overloading of the child's circulation with cells by transfusion instead of dilution of the plasma which should have been done, and it was only after this balance had been restored by giving large amounts of water and of a 5 per cent solution of dextrose in physiologic solution of sodium chloride that the patient began to take feedings properly and the number of bowel movements was reduced.

Several other patients have shown what can be accomplished in apparently hopeless cases by appropriate measures directed toward dilution of the blood; the history of M. R. serves to illustrate this point.

The child, M. R., was admitted on September 25, markedly undernourished. Examination of the blood showed: hemoglobin, 88 per cent; red cells, 4,860,000. The specific gravity of the serum was 1.029, and there was a cell percentage of 31. The patient was given a transfusion of blood and put on a formula. This resulted in only temporary improvement; the condition soon became very much worse. On September 29, the blood showed: hemoglobin, 97 mg. per hundred cubic centimeters; red cells, 5,780,000; specific gravity of the serum, 1.035 and percentage of cells, 47; this degree of concentration gave the blood such a dark color that the patient's skin and mucous membranes showed cyanosis. Despite intravenous and interstitial injection of a 5 per cent solution of dextrose, the condition remained poor, with severe vomiting and diarrhea until October 9, when the cell-plasma ratio was practically 50:50. At that time she was given intraperitoneally injected blood serum, frequently repeated intravenous injections of 5 per cent dextrose in physiologic solution of sodium chloride and feedings of cereal made with evaporated milk thickened with barley flour (because of severe vomiting); following this there was rapid marked improvement both in the child's condition and in the blood picture, until at the time of discharge, on October 18, she was showing a rapid gain, with the blood picture entirely within normal limits. Because of this patient's extreme degree of marasmus, the early treatment was probably wrong, as we were trying to give food in too large quantities and were not giving sufficient fluid to prevent an increasing concentration of the blood. As soon as this was corrected by the administration of blood serum as well as the intravenous administration of dextrose and saline solution, combined with the feeding of thickened cereals, the vomiting ceased, and the diarrhea improved so quickly that it was possible to discharge the child within nine days.

Within recent years much attention has been directed toward the rôle of sinusitis, otitis media and mastoiditis as causative agents in this type of severe diarrheal disease, and much has been said and written on the subject. Consequently, we have paid special attention to the ears

of infants with such conditions, and have tried to determine what relation these infections have borne to the onset, as well as to the progress, of the gastro-intestinal symptoms. In our earlier cases the tendency was to perform paracentesis when there was even a suspicion of otitis if the child had a marked elevation of temperature. We found that on admission few of the patients showed otitis media, and in only two cases was the condition definitely diagnosed as mastoiditis prior to, or at the time of, admission. When otitis media developed, it occurred during the patient's stay in the hospital, usually after a few days or a week of acute illness, and when this complication did occur recovery was delayed or even prevented.

One of our patients was operated on for bilateral mastoiditis during convalescence from a severe case of diarrhea, with subsequent recovery; another was operated on during a recurrence of the illness (second admission), but he died following operation. A third patient was sent home with bilateral otitis media, because it was felt that the condition might subside, but was readmitted at a later date for operation. We feel that such infections are rather uncommonly the cause of the severe gastro-intestinal upsets that we observe, and, furthermore, that when it is possible to restore a normal blood balance in these patients by the administration of large amounts of water or other fluids and to reestablish feeding with sufficient rapidity so that they do not remain in a very weakened condition in the hospital for more than a few days, such infections can frequently be prevented and recovery thus be more rapid and certain. After giving large quantities of dextrose or saline over a short period of time, it has become our practice to use blood serum or whole blood in the most severe cases, depending on the red cell and hemoglobin levels at that time, so as to build up immunity to bacterial infection if possible. In respect to sinusitis, mastoiditis and otitis media, our observations seem to coincide with those of Wishart,[25] who made careful studies at the Sick Children's Hospital in Toronto over a five-year period and came to the conclusion that few of the cases of diarrhea were initiated by these conditions. In contrast to our findings may be cited those of numerous observers who have felt that sinusitis and mastoiditis played a large part in the causation of this type of severe diarrhea, and have advised early paracentesis with opening of sinuses or mastoids; notable among these workers are Jeans and Floyd [26] and Holsclaw, Boehm and Bierman.[27]

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25. Wishart, D. E. S.: Relation of Infection of Ear and Infection of Intestinal Tract in Infants, J. A. M. A. **95**:1084 (Oct. 11) 1930.

26. Jeans, P. C., and Floyd, M. L.: Upper Respiratory Infection as Cause of Cholera Infantum, J. A. M. A. **87**:220 (July 24) 1926.

27. Holsclaw, F. M.; Boehm, C. A., and Bierman, J. M.: Otitis Media and Mastoiditis in Infants Under Three Months of Age, Am. J. Dis. Child. **39**:747 (April) 1930.

Vomiting was a symptom that was present in nearly all of our patients, often being emphasized by the parents more than the accompanying diarrhea. It varied in severity from occasional vomiting to an extreme type in which the vomitus consisted of fairly bright blood or coffee-ground material, mixed with thin, watery fluid or bile-stained mucus. Once or twice the diagnosis of high intestinal obstruction was seriously discussed because of fecal material and bile in the vomitus of children who were admitted in a state of collapse. Persistence of

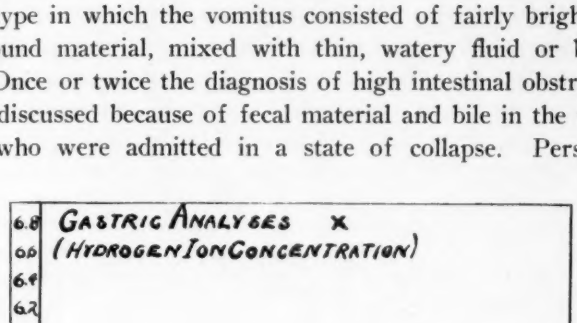

Chart 2.—Range of hydrogen ion concentration as shown by gastric analyses made on patients with diarrhea on admission, during the acute stage and on discharge from the hospital.

projectile vomiting in one instance called attention to the presence of a pyloric tumor in a child admitted primarily because of severe diarrhea.

We have made many analyses of gastric contents during the stage of acute illness, during convalescence and just prior to discharge from the hospital, using a standard test meal of 40 cc. of unsweetened evaporated milk, 80 cc. of water and 1.5 Gm. of calcium caseinate, which was given at 6:15 a. m. The gastric contents were removed after a two-hour interval, treated with an appropriate indicator and the reading made with a colorimeter. If the child vomited during the period of digestion the test was discarded as being inaccurate. Tests of saliva or

duodenal contents were not made, as was done by Davison,[28] who showed that less than one third of such specimens were free from contamination, and that the presence of either saliva or duodenal contents would materially reduce the p_H readings. We found that the specimens varied in p_H from 3 to 6, while in most instances this variation ranged from 4 to 5. Several of the patients who were very ill and in whom vomiting was troublesome, showed gastric acid as high as 3, while in many who had recovered the readings consistently ran from 4.6 to 5. The few values that were exceptionally low were obtained in gravely ill infants in whom bile and pancreatic juice was likely to be regurgitated into the stomach. The p_H range in our average patient was thus seen to be as high or even higher than the mean values found by other observers in normal infants when the technic was approximately the same and the infants received dilutions of sweet milk or powdered milk.[29]

TABLE 5.—*Showing Accomplishment in Apparently Hopeless Case by Dilution of Blood*

Rowan, 5 wk.	Hemoglobin, Mg.	Red Cells	Serum Specific Gravity	Hematocrit: Cells, per Cent	Hematocrit: Plasma, per Cent	Gastric p_H
Sept. 25	88	4,860,000	1.029	31	69	Oct. 1; 5.2
Sept. 25 Blood transfusion						Oct. 2; 4.8
Sept. 29	97	5,780,000	1.035	47	53	
Oct. 6	93	5,740,000	1.034	51.5	48.5	
Oct. 6 Intravenous and intraperitoneal 5% dextrose solution						
Oct. 9	92	5,760,000	1.031	40.6	59.4	
Oct. 9 Intraperitoneal blood serum						
Oct. 11	83	5,100,000	1.028	33.3	66.7	

In view of the wide range of gastric p_H, we were led to add barium to a few of the test meals and to make several roentgenograms of its progress through the stomach. As we had assumed there might be considerable stasis of the food in the stomach because of the frequency of vomiting, we were rather surprised to note that in several subjects the barium began to leave the stomach in a very short time, with only a little residue after four hours, while in others it was so slow that there was a large residue at the end of the four-hour period. We hope to have the opportunity of making more extended and more detailed observations on a larger number of patients at a future date so as to

28. Davison, W. C.: Gastric Analyses in Normal Infants and in Those Convalescent from Diarrhea, Am. J. Dis. Child. **30**:23 (July) 1925.

29. Marriott, W. McK., and Davidson, L. T.: Acidity of Gastric Contents of Infants, Am. J. Dis. Child. **26**:542 (Dec.) 1923. Davidsohn, H.: Arch. f. Kinderh. **69**:239 (April) 1921. Babbott, F. L., Jr.; Johnston, J. A.; Haskins, C. H., and Shohl, A. T.: Hydrogen Ion Concentration of Gastric Contents of Infants, Am. J. Dis. Child. **26**:475 (Nov.) 1923.

correlate these observations (if possible), because the present series is too small to warrant definite conclusions. However we feel quite certain that gastric digestion and gastric acidity play only a part in the inability of this type of patient to retain food. It seems probable that a great deal of the vomiting is the result of the changes occurring in the blood; these changes of concentration by increased hydrogen ion content, deranged chemical balance and deficient oxygen-carrying power are reflected in increased irritability of the centers of the central nervous system. This is probably most often true during the stage of acute anhydremia and toxemia. The cessation of vomiting (as well as diarrhea) following the administration of adequate amounts of fluid is usually dramatic.

The type of formula seemed to make slight, if any, difference in the amount of vomiting, provided it was begun cautiously and was increased carefully. In most instances, we found our routine feeding satisfactory; this consists of diluted nonacidified, evaporated milk with calcium caseinate added to bring the protein content to approximately 3.5 per cent.

After the acute period is passed, attention should be directed to the question of the giving of food best suited to the infant's peculiar needs. In this connection it may sometimes be necessary to raise or lower the acidity of the food according to the ability of the child's stomach to elaborate sufficient hydrochloric acid.

We have also noted that during recovery some of the patients retained a hypersensitive condition of the alimentary tract so that a bowel movement and frequently vomiting occurred immediately after the giving of food, and this relationship could be determined only by observation on the part of the nursing staff. The administration of antispasmodics, such as atropine or phenobarbital, if necessary, combined with thick feedings made by adding barley flour to the formulas, quickly caused cessation of symptoms, with a resulting rapid recovery. Following the relatively short period during which food by mouth has been stopped and fluids have been pushed by other routes, a properly diluted formula must be started as soon as possible to minimize loss of weight. It is probably equally, or more, important to begin the use of this formula sufficiently carefully to avoid overtaxing a gastro-intestinal mechanism that has not yet fully recovered its normal state. Any selected formula must be started in small, well diluted quantities and the infant's reaction carefully noted, otherwise a serious or even fatal relapse may be precipitated.

During the period of observation some patients were given protein milk and others, 2 per cent lactic acid milk, but most of them were given evaporated milk, sweet or acidified, according to the indications

under various circumstances. When the hydrogen ion concentration of the stomach was found to be very low, we used the evaporated milk formulas acidified by hydrochloric acid according to the formula of Faber [30] or lactic acid according to Marriott's formula. Except for these special formulas, the routine feeding given was unsweetened, evaporated milk, the dilution varying according to the individual case and to the stage of illness; usually it was started at one-half or two-thirds strength with calcium caseinate added to bring the protein content to about 3.5 per cent. As soon as possible, added carbohydrate was given in the form of dextrimaltose, corn syrup or barley flour. We found also that added calories, as well as protein, could be safely given by the incorporation of egg yolk in many formulas. As convalescence progressed, cereals were added to the diets of infants over 5 months. Most of our patients made satisfactory progress on the nonacidified, evaporated milk formulas; the color and consistency of the stools gradually returned to normal and the number decreased. Almost always after the severe loss of weight caused by the acute illness, there was a period during which the weight curve remained almost flat before a gradual rise began. Once the danger period apparently was passed, the children were sent home, their future course being followed in the outpatient department.

When home conditions were reasonably satisfactory, so that some degree of cooperation could be secured, nearly all of the babies gained well after leaving the hospital, and there were surprisingly few who came back with a recurrence of symptoms. This was particularly gratifying because it demonstrated that the patients could be sent home and fed the evaporated milk formulas, and that they continued to make excellent progress if supervised in the clinic. Because the formulas could be made with ease by the mothers, no change in feeding was necessary when the patient left the ward, and we felt that this was of the greatest importance, because change at such a time is always attended by considerable risk. Each mother was given a demonstration of the method of making the feeding before the baby was discharged from the ward; hence few mistakes were made in the preparation of food at home. Combining as it did, simplicity, digestibility and sterility, with moderate cost, evaporated milk seemed to make a particularly satisfactory type of feeding.

Examinations of the stools of twenty-three patients were made on one or more occasions, the material being obtained by means of a catheter passed into the lower part of the bowel so that the cultures could be made from fresh material within a few minutes of the time it was col-

30. Faber, H. K.: Hydrochloric Acid Milk in Infant Feeding, Am. J. Dis. Child. **26**:401 (Nov.) 1923.

lected. In only two instances in this group was a strain of the dysentery bacillus isolated, while in three others, a short chain streptococcus was isolated, alone or with other organisms. These five children were extremely ill, showed intense toxemia, and responded poorly to treatment, the stools being frequent, watery and containing blood mixed with mucus. From the cultures obtained from the remaining eighteen patients, we were unable to differentiate organisms not normally found in the intestinal tracts of the infants, e. g., B. coli and B. lactis-aerogenes, as well as various forms of staphylococci and diplococci. The reports found in the literature relating to the bacteriology of the stools from infants with diarrhea showed great variation as to the number of those in which the dysentery bacillus was found. The lack of uniformity seemed to depend on: (1) the technic used in procuring material for culture, (2) the type of patients under observation, (3) seasonal variation in incidence of dysentery infections and (4) locality. This may be illustrated by figures from the Babies' Hospital (New York) in 1903, when 35 per cent of the stools were positive; in 1923 (Wollstein [31]), only 23 per cent were positive, while in cases of ileocolitis at Johns Hopkins Hospital in 1920, 83 per cent were found positive (Davison [32]). In mixed groups such as ours, the incidence of true bacillary dysentery seems comparatively low, and with the present bacteriologic methods, no single organism can be picked out as a cause of diarrhea.

SUMMARY

Infants in whom acute diarrhea develops in the late summer show intoxication after a variable length of time when improperly or inadequately treated. The intoxication is the result of several factors—anhydremia, acidosis and bacterial toxins, the last occurring particularly when the intestinal tract has been invaded by such organisms as the bacillus of dysentery or the streptococcus. Patients with such a condition require prompt and energetic treatment if life is to be saved. During this critical period their chief requirement is water, and in this study we have endeavored to show to what extent the blood stream may be depleted of its fluid with a corresponding concentration of the cellular elements, electrolytes and protein. We feel that for satisfactory results each patient must be individualized, and that the foregoing laboratory procedures are of great value if treatment is to follow a rational course. Fully realizing that there are many complex factors to be taken into consideration, we have made use of only the methods that seemed to offer the most practical help, and we have constantly

31. Wollstein, M.: Bacteriologic Study of Acute Diarrheas in Young Children, Am. J. Dis. Child. **25**:310 (April) 1923.

32. Davison, W. C.: Bull. Johns Hopkins Hosp. **31**:225 (July) 1920.

borne in mind that such gravely ill infants must be subjected to a minimum of handling and trauma.

When it is possible to continue the child's care through the outpatient department, after the most acute period is passed, many complications may be avoided, as the patient is not surrounded during convalescence by the virulent bacteria that are inevitably present in a busy hospital devoted to the care of children. While undoubtedly mastoiditis and allied infections may be the cause of severe diarrhea, they were encountered in our patients as complications or sequelae.

Unsweetened evaporated milk, diluted to one-half or two-thirds strength, with protein or carbohydrate additions, proved to be a satisfactory formula for most of our patients as soon as they were able to take milk; however, here again a certain amount of discretion must be used in each case because of the degrees of variation found in the hydrogen ion concentration of the stomach contents and in the individual child's reaction to food. The evaporated milk formulas can be readily adjusted in percentage, acidity and consistency to meet these special requirements.

CONCLUSIONS

1. Observations made on a series of forty-eight patients suffering from diarrhea are presented.

2. Readings were made of serum-specific gravity, cell-plasma ratio (hematocrit tube) red cell count and hemoglobin and frequently on total blood chlorides as well, whenever possible at the time of admission, during the acute illness in the hospital and on discharge.

3. We feel that such data are of great value in outlining the course of treatment as well as in checking the clinical progress of the patient.

4. Routine feedings of diluted, unsweetened, evaporated milk, with added protein or carbohydrate, were satisfactory in most cases.

5. There was no constancy in the bacteriologic observations in the stools from these infants.

6. Otitis media, mastoiditis and sinusitis did not appear to be important etiologic factors in our series.

7. Most specimens of gastric contents showed a hydrogen ion concentration of from 4 to 5, with exceptional instances as high as 3 and as low as 6.

DISTURBANCES OF GROWTH IN CHRONIC ARTHRITIS IN CHILDREN

JOHN G. KUHNS, M.D.
AND
LORING T. SWAIM, M.D.
BOSTON

Chronic illness in children often produces a retardation in growth. This retardation is usually temporary, the growth process proceeding again normally with convalescence. The slowing of growth in such cases has been attributed to a conservation of the available energy of the child in the struggle to overcome the disease. Thursfield [1] regarded it as a lack of the available material that normally would be built into the growing tissues. The same explanation has been given for the slowness of growth often seen in severe malnutrition. However, as he also mentioned, adequate growth requires the proper proportion and distribution of the material for growth and adequate stimulus (Stefanescu [2]) for its utilization. For this Thursfield postulated a proper functioning of the glands of internal secretion. The commoner disturbances in growth resulting from dysfunction of the endocrine glands have frequently been described (Mau; [3] Ravina; [4] Lawrence; [5] Talbot [6]).

There are other diseases that disturb growth in a more serious manner by an involvement of the bones themselves. Chief among these are tuberculosis and rickets. In 1869, disturbances of growth in tuberculosis were first carefully described by Langenbeck,[7] who observed that disease in the joints of the lower extremities frequently produced a decrease in growth. Dollinger [8] studied 41 cases of tuberculosis of the knee joint, and found that retardation in growth occurred only when the disease became quiescent. In active tuberculosis, he found that the diseased leg kept up with the normal one, or sometimes grew even faster.

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From the Robert Breck Brigham Hospital.

1. Thursfield, H.: Brit. M. J. **1**:841, 1923.
2. Stefanescu, S.: Compt. rend. Soc. de biol. **95**:790, 1926.
3. Mau, C.: Deutsche med. Wchnschr. **49**:751, 1923.
4. Ravina, A.: Presse méd. **34**:1128, 1926.
5. Lawrence, C. H.: Boston M. & S. J. **191**:157, 1924.
6. Talbot, F. B.: Studies in Growth of Untreated Mongolian Idiots, Am. J. Dis. Child. **28**:152 (Aug.) 1924.
7. Langenbeck, B.: Berl. klin. Wchnschr. **6**:265, 1869.
8. Dollinger, J.: Centralbl. f. Chir. **149**:897, 1888.

An increase in the length of the long bones after tuberculous infection of the joints was also noted by Reschke.[9] Likewise, Pels-Lensden [10] found that a chronic tuberculous inflammation of the knee in children usually produced a lengthening of the limb during the time the disease remained active. Similar disturbances of growth have been observed in cases of osteomyelitis.

In 1853, Virchow [11] reported that in cases of rickets the diaphyses of the long bones often remained shorter than usual. Humphray [12] measured a series of rachitic femora and found that they were usually shorter than nonrachitic ones of the same age. As the pathologic changes that occurred at the zone of provisional calcification became more clearly understood, it was readily seen how disturbances of growth could be produced in this disease. The recent studies on renal rickets have shown a pathologic picture similar to that of rickets (Paterson;[13] Lathrop;[14] Smith and Walsh [15]). Parsons,[16] in an extensive study, found stunting in growth to be constant in renal rickets.

These conditions have been reviewed by way of preface because chronic illness, endocrine dysfunction and disease of the bones are all commonly found in chronic arthritis in children. Chronic arthritis in children, or Still's disease, as it is called, is not common, as most of the students of this problem have observed. In a series of 314 patients admitted for chronic arthritis to the Robert Breck Brigham Hospital, between 1922 and 1930, only 13 were under 12 years of age. The first description of chronic arthritis in children was that by Cornile [17] in 1864. Still,[18] in 1897, studied 22 cases. He stated: "A remarkable feature in these cases is the general arrest of development that occurs when the disease begins before the second dentition. A child of twelve and one half years would easily have been mistaken for one of six or seven years." He found this arrest in development to be wholly one of growth. However, a number of investigators, as Moncorvo,[19]

9. Reschke, K.: Deutsche Ztschr. f. Chir. **168**:136, 1922.
10. Pels-Lensden, F.: Deutsche Ztschr. f. Chir. **51**:257, 1899.
11. Virchow, R.: Arch. f. path. Anat. **5**:409, 1853.
12. Humphray, G. M.: Med.-Chirug. Soc. Trans., London **45**:27, 1862.
13. Paterson, D.: Brit. J. Child. Dis. **18**:186, 1921.
14. Lathrop, F. W.: Renal Dwarfism, Arch. Int. Med. **38**:612 (Nov.) 1926.
15. Smith, D. C. W., and Walsh, M. D.: South. M. J. **20**:437, 1927.
16. Parsons, L. G.: Arch. Dis. Childhood **2**:1 and 198, 1927.
17. Cornile, A.: Mem. Soc. d. biol. **1**:3, 1864.
18. Still, G. F.: Med.-Chirug. Soc. Trans., London **130**:47, 1897.
19. Moncorvo, C. A.: Du rheumatisme chronique noueux des enfants et son traitement, Paris, 1890.

Jacobi,[20] Lacoze-Dori,[21] Stoye [22] and Spitzy,[23] all of whom wrote extensively on Still's disease, made no mention of disturbances of growth. This was probably because their cases were not observed for a sufficiently long period. In our cases, retardation in growth became evident in some instances only after the patient had been under observation for several years.

There has been occasional mention in the literature of delayed development following chronic arthritis in children. Vogt,[24] in 1878, stated that the closer an inflammatory process came to the epiphyses the greater was its ability to disturb growth. Diamontberger,[25] in 1891, mentioned the occasional retardation in the development of the lower jaw. Hoppe Seyler,[26] in 1903, reported a case of a 23 year old woman who had suffered from arthritis since the age of 7 years. He found that the limbs of this patient had attained about three fourths of the usual length. A case of arthritis in a 20 year old woman, in whom the disease began at the age of 6 years, was described by Algyogyi; [27] there was symmetrical body development, and the height was 4 feet and 11 inches (150 cm.). Dock [28] described the case of a 24 year old man dying from chronic interstitial nephritis, who had had arthritis since the age of 11 and whose limbs showed decrease in growth. Ibrahim,[29] in a monograph on chronic arthritis in children, mentioned that faulty development of the nails and teeth was a common finding, as were underdevelopment of the mandible and early ossification of the epiphyses. Saupe [30] reported a case of chronic arthritis in a 10 year old girl who had had the disease since the age of 2 years. This patient showed marked retardation in physical development, weighing only 39 pounds (17.7 Kg.).

The case of a 58 year old man, who had chronic arthritis which began at the age of 9 years, was described by Eleakin.[31] The patient was 5 feet (152.4 cm.) tall and weighed 110 pounds (49.9 Kg.). The striking feature in this case was the shortness of the forearms. Both

20. Jacobi, A.: New York M. Record **36**:53, 1889.
21. Lacoze-Dori: Étude clinque sur le rheumatisme noueux chez les enfants, Thèse de Paris, no. 329, 1882.
22. Stoye, W.: Ztschr. f. Kinderh. **41**:538, 1926.
23. Spitzy, H.: Ztschr. f. orthop. Chir. **11**:699, 1903.
24. Vogt, P.: Arch. f. klin. Chir. **22**:343, 1878.
25. Diamontberger: Du rheumatisme noueux chez les enfants, Lecrosnier et Babé, Paris, 1891.
26. Hoppe Seyler, G.: Deutsches Arch. f. klin. Med. **75**:320, 1903.
27. Algyogyi, H.: Mitt. d. Gesellsch. f. inn. Med. u. Kinderh. **6**:103, 1909.
28. Dock, G.: Am. J. M. Sc. **144**:469, 1912.
29. Ibrahim, J.: Ztschr. f. orthop. Chir. **15**:213, 1914.
30. Saupe, E.: Med. Klin. **17**:288, 1921.
31. Eleakin, S.: Ztschr. f. Kinderh. **33**:55, 1922.

upper arms measured 11¼ inches (28.58 cm.), while the right lower arm measured 7½ inches (19.05 cm.) and the left lower arm 7¾ inches (19.69 cm.). Kienboch [32] followed a case of chronic arthritis, which began at the age of 8 years, from the thirty-first to the sixty-second year of life, when the patient died from an esophageal carcinoma. This patient was 46½ inches (118.11 cm.) tall and weighed 51 pounds 23.1 Kg.). The occipitofrontal circumference was 20 inches (50.8 cm.). Marinesco and Claudian [33] recently mentioned the dwarfism that may occur in children suffering from arthritis.

Various theories have been advanced to explain the disturbances of growth that occur in chronic arthritis in children. One of the earliest was that the limb does not grow at the normal rate because it is not used (Volkmann; [34] Johannsen [35]). That lack of proper function, with its accompanying circulatory disturbance (Ollier [36]), plays a rôle in disturbed growth has long been known to surgeons. Wolff,[37] in discussing disturbances of growth in all types of diseases of the joints, expressed the belief that a trophic disturbance was the primary cause, and that a disturbance in the nutrition of the epiphyseal tissues was secondary. That circulatory disturbances at the epiphyseal line alone can produce a change in growth was demonstrated by Broca [38] in 1856, and was shown again in a recent paper by Harris.[39] Endocrine disturbance, particularly thyroid deficiency, was suggested by Jockwer.[40]

While all of these factors—disuse of the limb, lack of circulation, trophic disturbance and thyroid deficiency—may at times play some part in the disturbances of growth in chronic arthritis, the chief cause, as suggested by Dock [28] and described by Kienboch,[32] has been the injury to the proliferating epiphyseal cartilages at the ends of the long bones. Belchier [41] and John Hunter, in the middle of the eighteenth century, proved conclusively that growth in length in the long bones occurs only at the epiphyses, and that it ceases when the epiphyses become ossified and united to the shaft of the bone. Epiphyseal damage and epiphyseal necrosis are common findings in all types of disease of the joints in children (Axhausen [42]). There have been few reports

32. Kienboch, R.: Fortschr. a. d. Geb. d. Röntgenstrahlen **40**:813, 1929.
33. Marinesco, G., and Claudian, I. F.: Arch. de méd. d. enf. **32**:633, 1929.
34. Volkmann, R.: Arch. f. klin. Chir. **9**:193, 1868.
35. Johannsen, N.: Acta paediat. **2**:354, 1923.
36. Ollier, L.: Rev. de chir. **1**:785, 1881.
37. Wolff, J.: Berl. klin. Wchnschr. **20**:422, 1883.
38. Broca, P.: Des anéurysmes et de leur traitement, Paris, Labé, 1856.
39. Harris, H. I.: J. Bone & Joint Surg. **12**:859, 1930.
40. Jockwer, W. E.: Arch. f. Kinderh. **82**:273, 1927.
41. Belchier, J.: Phil. Tr., London **39**:287, 1736.
42. Axhausen, G.: Arch. f. klin. Chir. **129**:341, 1924.

of pathologic changes in the bones and cartilage in arthritis in children. Still [18] made no mention of such changes in three cases that came to autopsy. Dock [28] mentioned partial destruction of the articular cartilages in his case. Koeppe [43] found thickening of the joint capsule and almost complete disappearance of the joint cartilage in a child aged 3½ years. Jockwer [40] reported two cases from the literature in which the joints showed thickened synovial membrane, fibrous ankylosis, marked atrophy of the bones, thinning of the articular cartilages, enlargement of the marrow cavities and almost complete ossification of the epiphyses.

The most complete description of the gross and microscopic pathologic conditions in the bones and joints in such cases was given in 1909 by Nichols and Richardson.[44] They found thickening and villous formation in the synovial membrane with proliferation from the membrane of a pannus-like layer of granulation tissue which gradually covered and eroded the cartilage. At the same time, proliferation of the connective tissue in the marrow cavity occurred below the zone of the provisional calcification. This vascular connective tissue grew toward the joint, ultimately destroying the cartilage in some cases. Following this, irregular formations of cartilage and bone took place, probably as a partial reparative process. In this manner, an injury, with premature ossification and union of the epiphysis, was produced. These pathologic changes in cartilage and bone, which are always present in varying degree, are, we believe, the most important cause of disturbances of growth (fig. 1).

A standard is necessary in order to measure retardation in growth. For major disturbances in growth and physical development, the most reliable tables in the United States are those compiled by Baldwin [45] and his co-workers. There are so many factors that may influence growth that slight variations are usually not of great significance. Schwalbe [46] has set 5 feet (150 cm.) as an arbitrary lower limit for normal growth in height. Todd [47] has analyzed growth and has divided it into two phases: (1) increase in dimensions and (2) modification in proportions. The increase in dimensions progresses fairly uniformly, with occasional spurts of growth, and ceases between the eighteenth and nineteenth year, with the closure of the cranial sutures and the union of the epiphyses with the shafts of the long bones. The modification in the proportion of the parts of the body continues throughout life, and, according to Todd, is the best index of chronological age, since it is not influenced by heredity or nutrition.

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43. Koeppe, H.: Jahrb. f. Kinderh. **76**:707, 1912.

44. Nichols, E. H., and Richardson, F. L.: J. Exper. Med. **16**:149, 1909.

45. Baldwin, B. T.: Use and Abuse of Weight-Height-Age Tables as Indexes of Health and Nutrition, J. A. M. A. **82**:1 (Jan. 5) 1924.

46. Schwalbe, quoted by Tallquist, T. W.: Acta med. Scandinav. 7:74, 1924.

47. Todd, T. W.: Northwest Med. **27**:165, 1928.

In children suffering from chronic arthritis, three types of disturbance of growth may be observed: 1. There may be a generalized retardation of growth, producing the physical characteristics of the dwarf, but with normal mental development and normal development of the reproductive

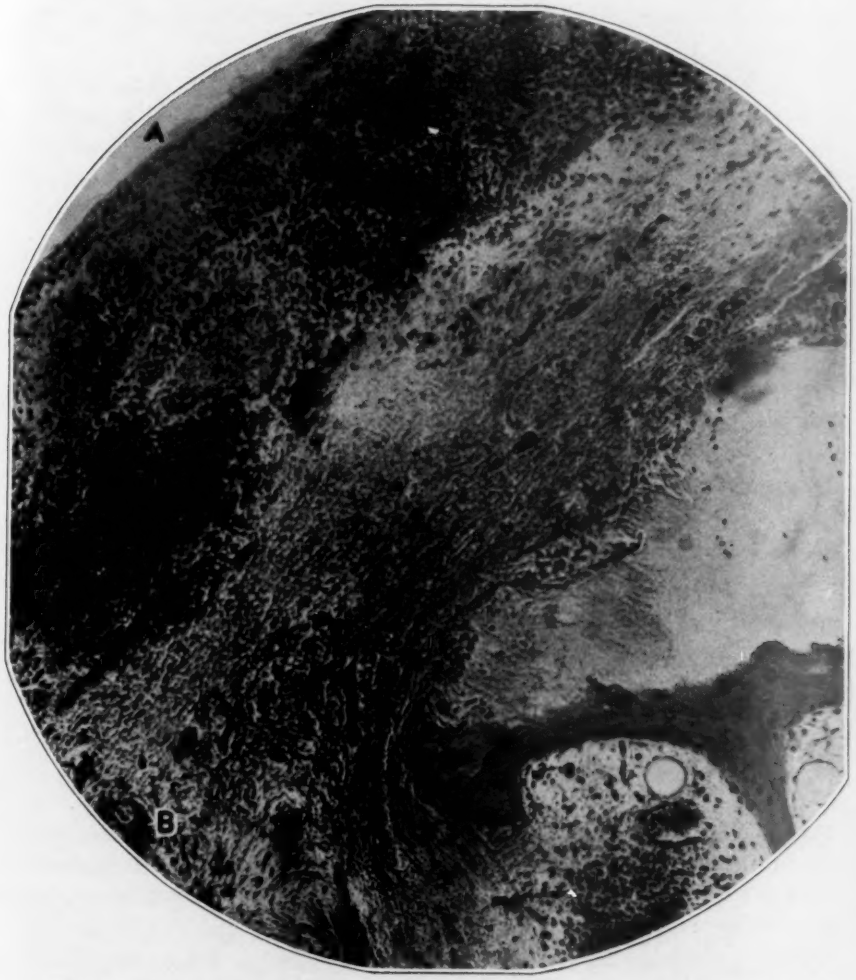

Fig. 1.—Photomicrograph of the end of a bone from a case of chronic arthritis, showing (*A*) overgrowth and invasion of the cartilage by pannus, and (*B*) encroachment of granulation tissue from the marrow cavity on the bony trabeculae and cartilage.

organs (Hill [48]). Fortunately, this type of disturbance of growth in chronic arthritis is very rare. 2. The second type is the persistence of infantile proportions and infantile appearance in the extremities. This

48. Hill, H. G.: Practitioner **125**:97, 1930.

is the most common type, and it can be seen in varying degree in most cases of chronic arthritis that are followed through the growing period. 3. The third type is an asymmetry in growth—a shortening of a limb, or a part of a limb, or symmetrical shortening of both limbs. The authors have observed all of these types. The type of disturbance of growth that will be produced depends on chance location and on the severity of the arthritis.

In the accompanying table we have tabulated the height, weight, occipitofrontal circumference, sex, age, and duration of the disease in twelve cases which are still under observation. In another case not recorded, the patient died three years after the onset of the disease, of chronic interstitial nephritis. Comparative normal values are given for height, weight and occipitofrontal circumference. Eleven of these

Comparative Study of the Twelve Patients in Our Series

		Age, Years	Duration of Disease, Years	Height, Inches	Weight, Pounds	Occipito-frontal Circum-ference, Inches	Normal Measurements: Height,* Inches	Normal Measurements: Weight,* Pounds	Normal Measurements: Occipito-frontal† Circum-ference, Inches
1.	♀# (Case 3).....	13	9	59½	83	20⅞	53	71	22.0
2.	♀ (Case 2).....	23	15	60¾	128½	22¼	..	..	....
3.	♀ (Case 4).....	22	14	60	98¾	23	60	111	22.0
4.	♀ (Case 1).....	16½	13½	50¾	79½	22⅛	59	104	22.0
5.	♀.....	14	11	59¼	72⅝	21	55	78	20.7
6.	♀.....	12	9	55	69½	20½	50	62	20.5
7.	♀.....	8	5½	47½	46¼	20¼	43	41	20.0
8.	♀.....	14	5	59	81½	20	50	58	20.7
9.	♀.....	6	3	44½	45	20⅞	41	39	19.7
10.	♀.....	4	3	40	34½	20	38	35	19.2
11.	♀.....	5	2¾	40¾	32	19½	41	38	19.5
12.	♂.....	12	2	58	73	21½	50	58	20.7

* The figures for normal height and weight are from Baldwin's tables; the lowest figures for height and weight of persons of the same ages were taken.

† The figures for normal occipitofrontal circumference are chiefly from Holt: Diseases of Infancy and Childhood; the figures for normal children of the same ages were taken.

The symbols ♀ and ♂ represent female and male, respectively.

patients were girls. Ibrahim [29] collected 245 cases from the literature; in this group there were 154 girls, or 62 per cent, and 91 boys, or 41.4 per cent. From this table it will be seen that wide variations from normal are uncommon. The circumference of the head in all cases fell within normal limits. This is because bones laid down in membrane, such as the bones of the skull, do not suffer any disturbance in their normal development from arthritis. Unfortunately, there are no tables or formulas for determining the normal length of limbs, and it is here, particularly in the hands and feet, that disturbances in growth are found. In two children whom the authors have followed an uncommon deformity, malocclusion of the jaws, developed from retarded growth of the mandible as a result of arthritis of the temporomandibular joint. Four cases are reported in detail in order to illustrate more fully the various types of disturbances in growth.

TYPE I. DWARFISM

CASE 1.—A Hebrew girl, was 8 years of age on her admission to the hospital, and at the time of this report is 16½ years (fig. 2, *a*). The onset of the disease occurred at the age of 3 years, without any immediately preceding illness or injury. Swelling and stiffness developed in the wrists, fingers and right knee. There was gradual spreading of the disease, with development of deformities of the ankles, knees, spine, shoulders and elbows. The patient had been treated elsewhere with autogenous vaccine and baking and massage of the joints, which brought no improvement. The past history was unimportant except for frequent attacks of sore throat prior to tonsillectomy and adenoidectomy at the age of 4 years. The father died of multiple sclerosis at the age of 32. The family history was other-

Fig. 2.—*A*, photograph of the patient in case 1. Note the short forearms and the small hands and feet. *B*, photograph showing the infantile proportions in the hands and the short forearms of this patient; ulnar deviation of the hand, due to disproportion in radial and ulnar growth. (See fig. 5 *B*.)

wise irrelevant. The general physical examination gave negative results, except for decayed teeth, a slight rachitic rosary, enlargement of the liver (two finger-breadths below the costal margin) and slight enlargement of the spleen. Examination of the extremities showed fusiform swelling in the finger joints of both hands; the shoulders and knees were limited in motion, and the elbows, wrists and ankles were almost completely ankylosed. X-ray films showed marked atrophy of all bones, periarticular thickening and irregular growth of the epiphyses. The results of all laboratory tests were normal, including the Wassermann and tuberculin reactions.

The patient remained in the hospital for four years. Progress was delayed by acute nephritis. This partially disappeared, and the general condition improved.

Treatment consisted of general hygienic measures, rest, physical therapy and calipers to straighten the knees. Eight years after the patient's first admission an arthroplasty was performed on the left elbow, and both wrists were manipulated (figs. 2 *B* and 3).

At the time of this report the child walks with crutches and calipers, and is able to feed and dress herself. X-ray films show: marked atrophy of all bones; marked narrowing of the articular spaces at the hip joints; fusion of the articular facets in the cervical region, and ankyloses at the right elbow, wrists and carpal and tarsal joints. Laboratory tests are all negative except that the urine shows a trace of globulin and a few hyaline casts.

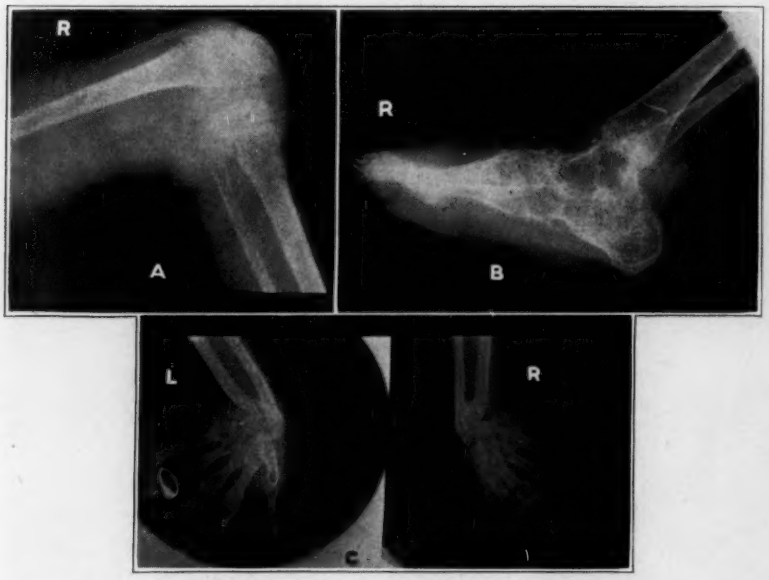

Fig. 3 (case 1).—Roentgenograms taken in 1929. *A*, the right knee; *B*, the right foot, and *C*, the hands (left hand at left of picture)—showing obliteration of the articular spaces; marked bone atrophy and premature union of the epiphyses, and early ossification of the ulnar epiphysis with disproportionate growth.

The measurements of the patient are as follows: height, 50¾ inches, weight, 79½ pounds (36.1 Kg.); occipitofrontal circumference, 23¼ inches.

	Right, Inches	Left, Inches
Femora	13	13
Tibiae	12⅝	13¼
Feet	6	6
Humeri	10	10
Ulnae	6⅞	6¾
Hands	4⅝	4⅝

The dwarfism of this child, with lack of growth in many bones, was due to early union of the epiphyses. The arthritis was extensive and severe, affecting general nutrition as well as particular epiphyses.

TYPE II. INFANTILE PROPORTIONS OF HANDS AND FEET

CASE 2.—An American girl, was 13 years of age on admission to the hospital, and at the time of this report is 23 years (fig. 4). The arthritis began at the age of 8 with severe frontal headaches. The face gradually became drawn toward the left side. This was followed by swelling and stiffness in the ankles and fingers. The disease spread and deformities appeared in the knees, feet and hands. No foci of infection were found. The patient's general health had never been good. An

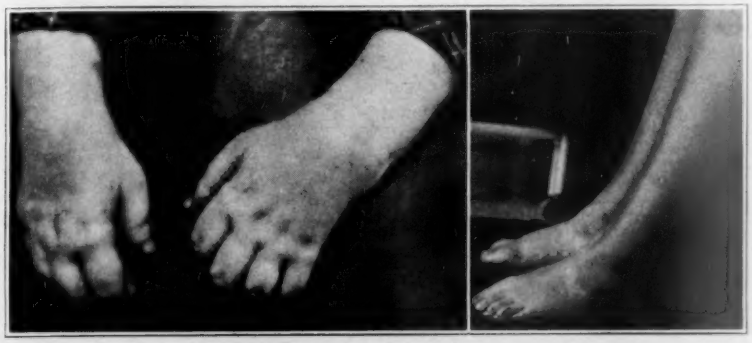

Fig. 4 (case 2).—Hands and feet. Note the infantile proportions; symmetrical type.

Fig. 5 (case 2).—Roentgenograms of the hands: *A*, taken in 1922, at the age of 14. Note atrophy, fusion of the carpal bones and absence of epiphyses. *B*, taken in 1929. There has been no growth.

obstetric paralysis of the right arm occurred at birth. She had influenza at 11 years. The family history was entirely unimportant.

General physical examination gave negative results, except that the tonsils were moderately enlarged. Examination of the extremities showed an obstetric paralysis of the Erb-Duchenne type of the right arm; both wrists were swollen and stiff in plantar flexion; the fingers contracted in flexion; both knees were flexed and partially subluxated. The head was held rotated to the left; no motion was possible in the cervical spine. The laboratory observations were all negative. X-ray films showed: generalized atrophy of the bones; distortion of the epiphyses at the wrists, knees and ankles; moderate periarticular thickening, and fusion of articular facets in the cervical spine.

The patient gradually improved under rest, physical therapy and general upbuilding measures. The knees were gradually straightened by traction and plaster casts. Tonsillectomy was performed one year after admission. Catamenia began at the age of 14. The patient began to walk with calipers, and from that time on improvement was continuous. Arthroplastic operations were performed on the left elbow and the left knee. Both hips were manipulated, with subsequent improvement in function.

The patient is a student in an art school at the time of this report. All laboratory tests are negative. X-ray films show: generalized atrophy of bone, marked narrowing of the articular spaces at the shoulders and hips and ankylosis of the carpal and tarsal bones (fig. 5).

The measurements of the patient are as follows: Height 50¾ inches; weight, 128½ pounds (58.3 Kg.); occipitofrontal circumference 22¼ inches.

	Right, Inches	Left, Inches
Femora	14¾	15¼
Tibiae	14	13⅞
Feet	6½	6⅝
Humeri	11⅝	11½
Ulnae	7½	8¼
Hands	6½	6⅝

Some of this difference in the proportion of the bones is due to operative procedures carried out for the correction of deformity and improvement of function, but the small size and infantile proportions of the hands and feet are a characteristic disturbance of growth. The patient has exceptional mental ability.

TYPE III. ASYMMETRICAL DISTURBANCE IN GROWTH

CASE 3.—An Irish girl, was 5 years of age on admission to the hospital, and at the time of this report is 13 years. At the age of 3½ years, without preceding injury or illness, a right-sided limp was noticed, which was followed by swelling of the right knee. Eleven months later the left knee became swollen, and shortly thereafter swelling occurred in the finger joints. There was no treatment except with medicines at home. The child had presented a difficult feeding problem until the age of 14 months. There were suppurative cervical adenitis at 18 months and again at 23 months and otitis media at 3 years. The family history was unimportant. General physical examination gave negative results except that there were dental caries, enlarged tonsils and generalized adenopathy, and the liver was palpable 3 cm. below the costal border. Examination of the extremities showed both feet to be in equinus deformity and both knees swollen, flexed and subluxated posteriorly. All laboratory examinations gave negative results. X-ray films showed: marked atrophy ot all of the bones, periarticular thickening at the left wrist and partial destruction of the articular cartilage at the left knee. The patient was put to bed and built up with rest, diet and physical therapy. The knees were gradually straightened with caliper splints. Improvement was constant, except when an operation was performed to correct faulty alinement of a supracondylar fracture of the left leg sustained through a slight fall. Seven years after her first admission, the patient was readmitted because of pain and stiffness in the left hip. Measurements at this time showed the left leg to be 1 inch shorter than the right. The hip gradually became quiescent. The generalized glandular enlargement

disappeared, and the liver was no longer palpable. The patient is now at home, walking with crutches. All laboratory examinations at the time of the present report give negative results, except the tuberculin reaction, which is positive. X-ray films show moderate increase in density of the bones. There is marked narrowing of the articular space at the left knee. The left femur is much smaller than the right. There is a destructive lesion with partial healing in the acetabulum and femoral head at the left hip joint (fig. 6).

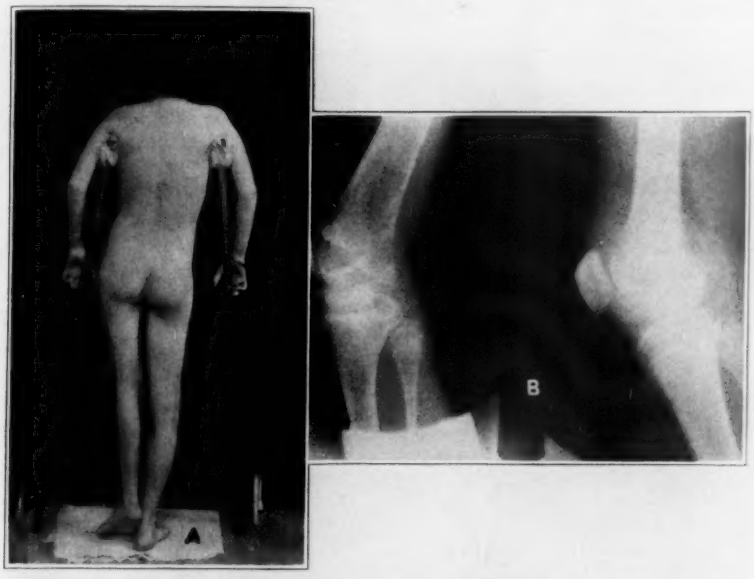

Fig. 6.—*A*, photograph of the patient in case 3. Note shortness of the left leg, due to early ossification of both femoral epiphyses. *B*, roentgenograms taken in 1929 showing the knees of this patient. Note the small femur and tibia on the left and the distortion and ossification of the epiphyses.

The measurements of the patient were as follows: height, 59½ inches, weight, 83 pounds (37.6 Kg.); occipitofrontal circumference, 20⅞ inches.

	Right, Inches	Left, Inches
Legs (anterior superior spine to internal malleoli)	30¾	28½
Femora	16⅞	15
Tibiae	14¼	13⅞
Feet	9	8¼
Humeri	10⅜	10⅝
Ulnae	9⅜	9⅜
Hands	6½	6½

This case illustrates a less extensive arthritis than was present in the first two cases, with no generalized retardation. A few epiphyses ossified early, and the corresponding bones ceased to grow.

TYPE III. SYMMETRICAL SHORTENING OF EXTREMITIES

CASE 4.—An Italian girl, was 17 years of age on admission to the hospital, and at the time of this report, is 22. At the age of 9 years, without any fever or preceding injury, the patient began to have swelling of both ankles. This was followed by swelling of both wrists. Until her admission to the hospital, eight years later, there were recurrent exacerbations of pain and swelling; with periods in bed alternated with periods of almost normal activity, but the condition gradually became worse until the patient was bedridden. There was no treatment except

Fig. 7.—*A*, photograph of the patient in case 4. Note shortness of the upper extremities. *B*, roentgenogram of the left knee taken in 1925. Note the ossification of the epiphyses, bone atrophy, rotation and subluxation. *C*, roentgenogram of the hands taken in 1925. Note the early ossification of the epiphyses in both extremities.

with medicines at home. Except for tonsillectomy at the age of 6 and appendectomy at 16, the past history was unimportant. Catamenia began at 13. The family history was irrelevant.

General physical examination revealed nothing abnormal. Examination of the extremities showed arthritis in all of the major joints. Motion of the lower jaw was limited to half the normal range. There was restriction of motion in the neck, shoulders, hips, knees and ankles. The elbows and wrists were ankylosed in

flexion. Laboratory observations were normal, except that there was a trace of albumin in the urine. X-ray films showed: marked atrophy of the long bones with partial destruction of their articular cartilages, dislocation of the metacarpophalangeal joints, ankyloses of the wrist joints and the carpal bones and thinning of the intervertebral fibrocartilages.

The patient was given rest, physical therapy and general upbuilding treatment. The knees were gradually straightened with plaster casts, and she was permitted to walk. Three years after admission, an arthroplasty was performed on the right elbow. This was followed by an arthroplasty on the left elbow, and later on the right knee. General improvement continued. At the time of this report the patient is at home; she walks, and there is no active arthritis. All laboratory examinations give negative results. X-ray films show a little increase in the density of the long bones (fig. 7). The measurements of the patient are: height, 60 inches; weight, 99½ pounds (45.2 Kg.); occipitofrontal circumference, 23 inches.

	Right, Inches	Left, Inches
Femora	13⅜	13½
Tibiae	11⅞	12
Feet	8	8
Humeri	10⅛	10¼
Ulnae	8½	8
Hands	6	6

The patient can walk. She has 60 degree motion in the hips, almost full use of the neck, back and elbows and 50 per cent use of the shoulders. The wrists are stiff; the fingers, useful. She presents an example of symmetrical early ossification of the epiphyses of the long bones of the extremities.

COMMENT

In these four cases one or more of the described types of disturbance of growth has occurred. We believe that the type and the extent of disturbance in growth depend on the severity and location of the disease, and are due to injury to the epiphyses with early ossification. This group of cases is far too small for the laying down of any rule, if there is any, as to interference with growth in chronic arthritis. In none of the cases under observation was there any clinical evidence of syphilis, and the Wassermann test in each case was negative. Elizalde and Pozzo,[49] as well as Acuña and Bazán,[50] believe that many instances of this type of arthritis are due to congenital syphilis. In none of our cases was there a suggestion of tuberculous infection except in case 3 in which the tuberculin test was strongly positive and in which there was a rapidly progressing lesion in the left hip joint, which has since become quiescent. Poncet,[51] in 1902, described a type

49. de Elizalde, P., and Pozzo, F.: Semana méd. **1**:455, 1923.

50. Acuña, M., and Bazán, F.: Semana méd. **2**:1159, 1924.

51. Poncet, A.: Bull. méd., Paris **16**:1057, 1902.

of arthritis occurring in adults and children, namely, a toxic or allergic involvement of the joints due to tuberculous disease in another part of the body. Piske,[52] Rhonheimer [53] and Poynton [54] mentioned tuberculosis as the possible causative agent in cases of Still's disease. While we have kept in mind both tuberculous and syphilitic infections, we have been unable to establish such diagnoses in any case.

A review of the literature offers little material on either the treatment for the disease or on the prevention of the disturbances that occur during the period of growth. The disease is not fatal, but in many cases does lead to severe crippling and invalidism. The only known way of preventing or allaying the disturbances that hinder growth is to make the arthritis quiescent. Practically all authorities are agreed that this can best be done by adequate rest, and by the use of whatever measures will improve the general condition of the child. These include an adequate diet, rich in vitamins and mineral salts; tonics, either drugs, particularly those that stimulate hematopoiesis, or sunlight or light therapy; endocrine products, when carefully controlled tests suggest an endocrine insufficiency; the removal of foci of infection, when the general condition of the patient permits such operative procedure; the use of vaccines and serums in selected cases with definite bacterial infection or allergic response, and corrective exercises to improve circulation, assimilation and elimination.

Locally, much can be done to prevent deformities (Swaim and Kuhns [55]) and disturbances in growth. If deformities do not occur, as they should not under proper care, a judicious alternation of rest and use will prevent much atrophy and circulatory stasis. Physical-therapy, in the form of baking and gentle massage, is helpful, both in maintaining muscle nutrition and strength and in relieving pain. But much more can be accomplished by active exercises. In certain cases operations will be required in order to restore motion. They should be performed only when the disease is quiescent and the general condition of the patient permits such a procedure. Our experience leads us to believe that the earlier treatment is started the better the results will be. Improvement in local circulation by means of heat is extremely valuable. Deep breathing and abdominal exercises have a marked effect in improving the general circulation. Local rest, alternating with guarded exercise, lessens atrophy and maintains almost normal nutrition of the limbs.

52. Piske, J.: Med. Klin. **48**:1968, 1913.

53. Rhonheimer, E.: Ergebn. d. inn. Med. u. Kinderh. **18**:531, 1920.

54. Poynton, F. J.: Lancet **1**:807, 1925.

55. Swaim, L. T., and Kuhns, J. G.: The Prevention of Deformities in Chronic Arthritis. I. The Upper Extremity, J. A. M. A. **93**:1853 (Dec. 14) 1929; II. The Spine and the Head, ibid. **94**:1123 (April 12) 1930; III. The Lower Extremity, ibid. **94**:1743 (May 31) 1930.

Such measures have proved most successful in lessening the severity of the disturbance of growth. Early ossification of the epiphyses, with resulting deformity, must be anticipated as an accompaniment of the arthritis, unless the arthritis can be stopped in its earliest stages. Children with arthritis, therefore, must be kept under observation for several years after the active stage of the disease is over.

CONCLUSIONS

1. Disturbances in growth are not uncommon in chronic arthritis in children. Such disturbances may appear only after several years of the disease, and are found oftenest in children with poor health and resistance.

2. These disturbances, while they are influenced by nonuse of the body and by nutritional and endocrine dysfunction, are due chiefly to the involvement of the proliferating epiphyseal cartilages, resulting in early ossification. They are dependent on the severity and chance location of the arthritis.

3. There are three general types of disturbances in growth in chronic arthritis. The commonest of these is the persistence of infantile proportions in the hands and feet. Shortness of an extremity or a portion of an extremity, or symmetrical shortening of both limbs, is fairly common. Dwarfism is relatively rare, but occurs in cases of severe, generalized arthritic involvement.

4. The prevention and cure of these disturbances rest, first, on general measures to combat the disease in its early stage and to improve the general condition of the patient as rapidly as possible, and second, on local measures to improve the function of the extremities and to promote circulation.

5. Every child with chronic arthritis should be observed at regular intervals for at least five years after the disease is quiescent.

Case Reports

DERMATOMYOSITIS

SAMUEL KARELITZ, M.D.
AND
SARA K. WELT, M.D.
NEW YORK

Polymyositis or dermatomyositis is a nonsuppurative, nonspecific inflammatory disease of the striated muscles and the surrounding areolar tissue. It frequently involves the skin and occasionally the mucous membranes and is characterized by pain, fever and edema. It may be acute, subacute or chronic.

In 1887, almost simultaneously, Hepp,[1] Unverricht [2] and Wagner [3] independently published reports of cases of this condition. Hepp called it "pseudo-trichinosis"; Wagner and Unverricht described it under the name of "polymyositis acuta progressiva." The morbid pathology of this type of disease was described about seventy years ago by Virchow. In 1891 Strümpell [4] collected ten cases from the literature and added one that he had observed. His clinical and pathologic descriptions of this entity are classic. Since Strümpell's report there have been several excellent treatises on the subject by Senator,[5] Lorenz,[6] Steiner,[7] Kader,[8]

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From the Department of Pediatrics, Mount Sinai Hospital.

1. Hepp: Ueber Pseudo-Trichinose, eine besondere Form von acuter parenchymatöser Polymyositis, Berl. klin. Wchnschr. **24**:297 and 322, 1887.

2. Unverricht: Ueber eine eigenthümliche Form von acuter Muskelentzündung mit einer der Trichinose ähnelnden Krankheitsbilde, München. med. Wchnschr. **24**: 488, 1887; Ztschr. f. klin. Med. **12**:533, 1887.

3. Wagner, E.: Ein Fall von acuter Polymyositis, Deutsches Arch. f. klin. Med. **40**:241, 1886-1887.

4. Strümpell: Zur Kenntnis der primären acuten Polymyositis, Deutsche Ztschr. f. Nervenh. **1**:479, 1891.

5. Senator: Ueber acuter Polymyositis und Neuromyositis, Deutsche med. Wchnschr. **19**:933, 1893.

6. Lorenz, H.: Die Muskelerkrankungen, Wien, A. Hölder, 1898, pp. 120 and 160.; Verhandl. d. Kong. f. inn. Med. **23**:243, 1906.

7. Steiner, W. R.: Dermatomyositis with Report of a Case, J. Exper. Med. **6**:407, 1905; Dermatomyositis, J. A. M. A. **78**:271 (Jan. 28) 1922.

8. Kader, B.: Klinische Beiträge zur Aetiologie und Pathologie der soganennten primären Muskelentzündungen, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **2**:41, 1897.

Oppenheim,[9] Rotky [10] and others. In the United States the first report on the subject was published in 1888 by Jacoby,[11] who called the condition "subacute progressive polymyositis." More recent reports on the subject, in this country, were made by Friedman,[12] Clowe,[13] Fox,[14] Joachim,[15] Moore and Koch [16] and others.

To date about seventy-five cases of this disease have been reported. It has been observed most frequently among males, usually of middle age and of varied nationalities. Twenty-two of the seventy-five cases occurred in childhood. Steiner's report in 1905 included twenty-eight authentic cases, with only two in children. In 1912 Rotky accumulated forty cases from the literature, among which were two in children. The only two cases occurring in childhood in the American literature are one reported by Steiner [17] and one by Moore and Koch.[16]

It is apparent that the disease has been observed rarely and by relatively few observers. It is possible that the condition occurs more frequently than it is recognized. Oppenheim, in his textbook on nervous diseases,[18] corroborated this impression by stating that in none of the ten cases referred to by him was the diagnosis made correctly.

ETIOLOGY

The etiology is still obscure, but the condition is generally considered to be of an infectious nature or a toxemia secondary to the infection. Bacteriologic examination made during the life of the patient and postmortem examination have failed to reveal the causative agent. Fox obtained a staphylococcus from the blood culture in a case of polymyositis. Batten's [19] and Rotky's [10] patients had negative blood cultures.

9. Oppenheim, H.: Ueber die Polymyositis, Berl. klin. Wchnschr. **40**:381 and 416, 1903; Zur Dermatomyositis, Berl. klin. Wchnschr. **36**:805, 1899; Lehrbuch der Nervenkrankheiten, ed. 2, Berlin, S. Karger, 1923.

10. Rotky, H.: Ueber Polymyositis acuta, Berlin, Urban & Schwarzenberg, 1912.

11. Jacoby, G. W.: Subacute progressive polymyositis, J. Nerv. & Ment. Dis. **15**:697, 1888.

12. Friedman, E. D.: Dermato-Myositis, M. J. & Rec. **123**:382 (March 17) 1926.

13. Clowe, C. F.: Acute Primary Polymyositis with Report of a Case, New York M. J. **92**:1177 (Dec. 10) 1910.

14. Fox, H.: Acute Polymyositis, Am. J. M. Sc. **145**:879 (June) 1913.

15. Joachim, H.: A Case of Dermato-Myositis, Arch. Dermat. & Syph. **7**:326 (March) 1923.

16. Moore, C., and Koch, L. A.: Dermatomyositis, Am. J. Dis. Child. **35**:71 (Jan.) 1928.

17. Stiener, W. R.: Dermatomyositis, Report of Two Cases, J. A. M. A. **78**: 271 (Jan. 28) 1922.

18. Oppenheim (footnote 9, third reference).

19. Batten, F. E.: Case of Dermatomyositis in a Child with Pathological Report, Brit. J. Child. Dis. **9**:247, 1912.

Senator [5] observed acute polymyositis in a man, 40 years of age, who had eaten tainted crabs, and assumed that the disease might have been caused by absorption of toxins from the intestinal tract. Kell [20] also reported having seen the disease in three sailors who had eaten fish. Strümpell pointed out that in some of the recorded cases, including his own, the patients had pulmonary tuberculosis, and he suggested a possible relationship between the two diseases. Sick [21] reported an epidemic of polymyositis in the psychiatric clinic in Tübingen, where nine female nurses were affected. Despite the fact that other nurses who ate the same food did not become ill, he suggested that the disease might have been caused by intestinal infection. Pfeiffer [22] suggested that the etiologic agent might be the protozoa Gregarina, the condition being analogous to "myositis gregarinosa" in some lower animals, but he failed to find the protozoa in specimens submitted to him from cases of Unverricht [2] and Strümpell.[4] McLester [23] offered the theory of Theobold Smith: "The disease may be due to the invasion of the muscular system with sarcosporidia from the animals, especially the pig. He believed that the reason the etiology had not been cleared up was possibly that these parasites on entering an aberrant host might have been unable to grow sufficiently for histologic recognition, but that the abortive growth might have lead to sufficient foreign protein to cause the inflammation of the muscle tissue."

Occasionally polymyositis follows an acute infectious disease. Schuller [24] reported polymyositis following pertussis in a boy, aged 7 years; and others have seen it subsequent to measles. Litten [25] and Soelders [26] have reported cases in which the condition followed poisoning with carbon monoxide.

Polymyositis due to syphilis, trichinosis or acute fulminating pyogenic myositis and that due to avitaminosis or to ergot poisoning are in all probabilities different diseases from dermatomyositis, and should be considered separately.

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20. Kell, J. B.: Report of Three Cases of Polymyositis Acuta, with Report of Post-Mortem on One Case, J. A. M. A. **26**:967 (May 16) 1896.

21. Sick: Akute rezidivierende Polymyositis in epidemischen Auftreten, München. med. Wchnschr. **52**:1092, 1905.

22. Pfeiffer, R.: Die Polymyositis respektive Dermatomyositis acuta, Centralbl. f. allg. Path. u. path. Anat. **7**:81, 1896.

23. McLester, J. S.: Dermatomyositis, J. A. M. A. **87**:1990 (Dec. 11) 1926.

24. Schuller, A.: Polymyositis im Kindesalter Jahrb. f. Kinderh. **58**:193, 1903.

25. Litten, cited by Lorenz, H., in Nothnagel, C. W. H.: Specielle Pathologie und Therapie, Vienna, A. Hölder, 1898, vol. 11, pt. 3, p. 160.

26. Soelders, cited by Oppenheim: Lehrbuch der Nervenheilkunde, Berlin, S. Karger, 1908.

PATHOLOGY

Macroscopic Pathology.—The involved muscles may be adherent to the surrounding skin and subcutaneous fascia. The muscles are usually soft and friable, but may be indurated, scarred and contracted and are grayish or pale yellow. Red patches indicating hemorrhagic foci may be seen. The epidermis is reduced in thickness. There is, in places, complete absence of papillae. Fat and subcutaneous areolar tissue are very much reduced and are replaced by fibrous tissue poorly supplied with blood vessels. In earlier stages the skin may be thick, owing to intercellular edema.

Microscopic Pathology.—Inflammatory and degenerative changes of the parenchymatous and interstitial tissue are present. The extent of these changes depends on the intensity and stage of the disease. Loss of striation, cleavage of the fibers, fatty hyalin, vacuolar degeneration, round cell infiltration and hemorrhage may be seen. Interstitial edema and leukocytic infiltration are regularly found. If the heart muscle is involved, the findings are similar to those in other striated muscles. The blood vessels are usually congested. In Batten's case there were perivascular infiltration of round cells, thickening of the blood vessel walls and occasionally obliteration of the vessels. One of our patients (case 1) showed a similar picture plus an involvement of the musculature of the blood vessels.

SYMPTOMATOLOGY

The onset is usually gradual, with a prodromal period lasting from several days to several weeks, during which there are malaise, headache, anorexia and rheumatoid pain. This pain may at first appear as muscular fatigue, drawing pains or even paresis of the extremities; later it becomes a severe ache as in rheumatism. It may be spontaneous, but is more frequently elicited by active or passive motion. The pain may arise in the vicinity of joints, but the joints are never affected. Only a few muscle groups may be involved at first, but the disease usually spreads rapidly, including all striated muscle. The muscles of deglutition and respiration may be affected, giving rise to aspiration pneumonia and even asphyxia. The muscles of the tongue and eye are only rarely involved. Occasionally the heart is implicated. Fever of every type and degree appears early or after several weeks, and may persist for months. About the time the fever appears the patient becomes bedridden, and the affected muscles become enlarged, firm, contracted and exquisitely tender. Chills occur rarely. Edema of the indurated type is almost invariably seen at this stage or earlier. It may first involve the lower eyelids. It then spreads symmetrically or asymmetrically over all affected parts, usually the entire body. The edema

produces a glistening of the skin and gives the face a masklike appearance. Occasionally pitting edema may also be observed.

The skin is involved in almost all cases. In addition to its being doughy, edematous and rather closely attached to the subcutaneous tissues, various manifestations may appear throughout the illness. Urticarial, purpuric, erysipeloid, multiform erythematous, nodular erythematous, pemphigoid, eczematoid and scarlatiniform eruptions have been observed. The cutaneous condition is usually an early symptom, and, like the edema, most frequently appears on the face and fluctuates in its severity throughout the illness. One of our cases (case 1) presented a butterfly-shaped erythema on the face so similar to lupus erythematosus that the lesion was regarded as of tuberculous origin. Pruritus, desquamation and profuse sweating may occur. The cutaneous lesions may vary in type in the same patient at one time; thus the patient in case 1 had simultaneously the lupus erythematosus-like condition mentioned, symmetrical purpuric lesions on the ankles and telangiectases on the knuckles and face. It is the cutaneous involvement that led Unverricht to name the disease "dermatomyositis." The mucous membranes of the mouth are frequently involved, as in case 1. Oppenheim called attention to lesions of the oral mucous membranes and suggested the name "dermato-muco-myositis." Senator reported a case with neuritic symptoms and called the condition "neuro-myositis."

The sensorium remains free, and there are usually no sensory disturbances other than marked tenderness over the involved muscle. Superficial reflexes may be normal, diminished or absent, depending on severity of muscular pain and involvement rather than on involvement of the nerves. Cardiac murmurs and changes in pulse may be observed. Myocardial involvement occurs, and when severe may result in heart failure. If the muscles of deglutition or respiration become involved, suffocation or aspiration pneumonia may result. Splenic tumor is frequently present, especially in the acute cases. The blood shows no chemical and usually no morphologic changes. As a result of the involvement of the skin, ulcerations in the folds of skin and decubitus ulcers occur and may, as in one of our cases, cause death by secondary infection. The urine is usually normal, but may contain some albumin and casts, especially during the febrile period.

PROGNOSIS

The prognosis of the disease is usually grave. Its duration is most frequently from six to eight weeks, but the condition has been reported as lasting over two years, with recovery in some cases and death in others. Recovery may take place in a few weeks. In twenty-eight cases collected by Steiner seventeen patients died. In two cases subsequently reported by him the patients died. Friedman's two patients

died. Of the eighteen children whose fate is known, seven died. Many of the surviving patients are left with atrophy and contractures of the muscles. Possibly this disease precedes some of the rare muscular diseases with fibrosis or calcification. Those who succumb most frequently die of some complication, such as aspiration pneumonia or terminal sepsis. Few deaths are the result of asphyxiation or myocardial involvement.

THERAPY

Treatment is entirely symptomatic and empiric and for the most part consists in physical therapy. Antirheumatic drugs, such as salicylates, and acetphenetidin have been recommended. During the very painful stage absolute rest in bed and splints to prevent contractures are indicated. Energetic diaphoresis brought about by thermomassage, infra-red rays or electrotherapy may be helpful. Those who believe that the disease is caused by intestinal toxins suggest thorough evacuation of the intestinal tract. Kroemer [27] used small doses of neoarsphenamine with a good result in a boy aged 16. Care of the skin is very important, since intertrigonous and decubitous ulcers are prone to occur and may become secondarily infected. When the acute stage of the illness has passed, passive and active motion and orthopedic measures are helpful and necessary.

Potassium iodide, neoarsphenamine, acetylsalicylic acid, colonic irrigations, yeast, cod liver oil, special diets rich in vitamins or high in carbohydrates, infra-red rays, ultraviolet rays, electric stimulation of the muscles, diathermy, a transfusion of 300 cc. of blood and other therapeutic measures were tried in case 1, causing only moderate improvement. How much of the improvement could be ascribed to treatment and what part to spontaneous healing during the eight months of the illness was difficult to decide. We were inclined to believe that good nursing and time helped most. Thyroid, restriction of fluids, a diet high in protein and most of the measures used in case 1 were employed in case 2. The patient in case 1 died of terminal sepsis from an infected decubitus ulcer, and the second patient made a slow but good recovery.

REPORT OF CASES

CASE 1.—Z. R., a girl, aged 6 years, was of Russian Jewish parentage. The family history was unimportant, and the patient's past history was uneventful except for a congenital strabismus and chickenpox at the age of 3 years. The present illness started about Aug. 4, 1929, when red streaks were noticed under both eyes. The areas of redness lasted one week, then spread lower down the face, crossing the nose and causing a butterfly-shaped erythema. Within two weeks there were marked anorexia and edema under both lower eyelids; the eruption

27. Kroemer, cited by Ibraham, Pfaundler and Schlossman: Handbuch der Kinderheilkunde, Leipzig, F. C. W. Vogel, 1924, vol. 4, p. 427.

spread over the extensor surfaces of all the extremities, and there were patchy areas on the buttocks. The diagnosis of lupus erythematosus was made, and ultraviolet ray treatment given, without any improvement. On Sept. 26, 1929, after increasing weakness, loss of weight, edema of the face and persistent cutaneous eruptions, the child was admitted to the Massachusetts General Hospital, where the diagnosis of lupus erythematosus was confirmed. A tuberculin test with a dilution of 1 : 1,000 was negative, and roentgenograms of the chest were suggestive of enlargement of the hilus gland. Tonsillectomy was done to remove a possible focus of infection. The patient was discharged on October 15, and sanatorium care was advised. On arriving home on October 15, the child first complained of being tired and unable to walk. This feeling became worse daily, as did the edema on

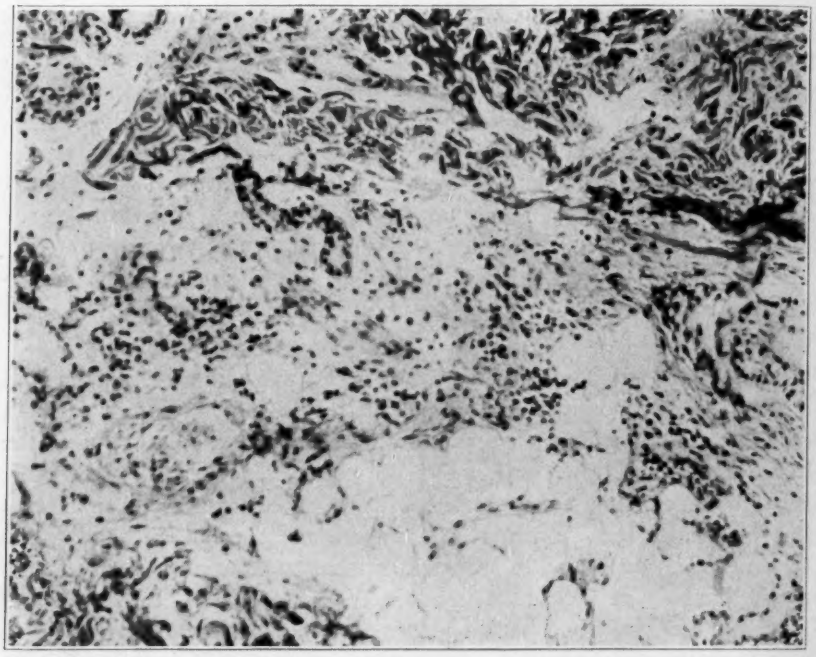

Fig. 1 (case 1).—Section through the skin and biceps muscle showing muscle fragmentation and separation of the fibers by edema. The dermis shows round cell infiltration and edema.

the face. Edema extended over the entire body. On October 22, the patient began to have a daily temperature of 99 F. in the morning and 101 F. in the afternoon. Gradually she became unable to move and cried with pain on being moved. She ached all over. A diagnosis of acute rheumatic fever was made, and three teaspoonfuls of cod liver oil and 60 grains (2.9 Gm.) of acetylsalicylic acid were given daily. The condition remained unchanged until about December 1, when her pulse rate suddenly rose from 100 to 120 to 160 to 180. A systolic murmur was heard, and several days later a diastolic murmur became audible. A cardiologist then concurred in the combined diagnosis of lupus erythematosus diffusa and acute rheumatic fever with endocarditis. About December 20 the temperature began to rise to 103 F. daily, despite the large doses of salicylates. The patient was seen

on December 29 by one of us (Dr. Karelitz). At that time there was a red erythema, butterfly shape, over the face and nose, and irregular over the dorsal aspects of the arms, elbows, wrists, thighs, knees, legs and ankles. The eruption was scaly and itched; it healed under the eyelids, leaving white areas of depigmentation. The edema was firm, indurated and brawny, and in places, doughy. There was no pitting. The child lay immobile, with marked tenderness on pressure or passive motion. She could not move any part of her body, except her face, without pain. Her pharynx and buccal membrane were red and raw, her gums were spongy and her tongue was geographic; her forehead was deeply pigmented brown; she had bilateral internal strabismus. The lungs were clear; the heart was not enlarged; the pulse rate was 140, and there were a soft systolic and a faint

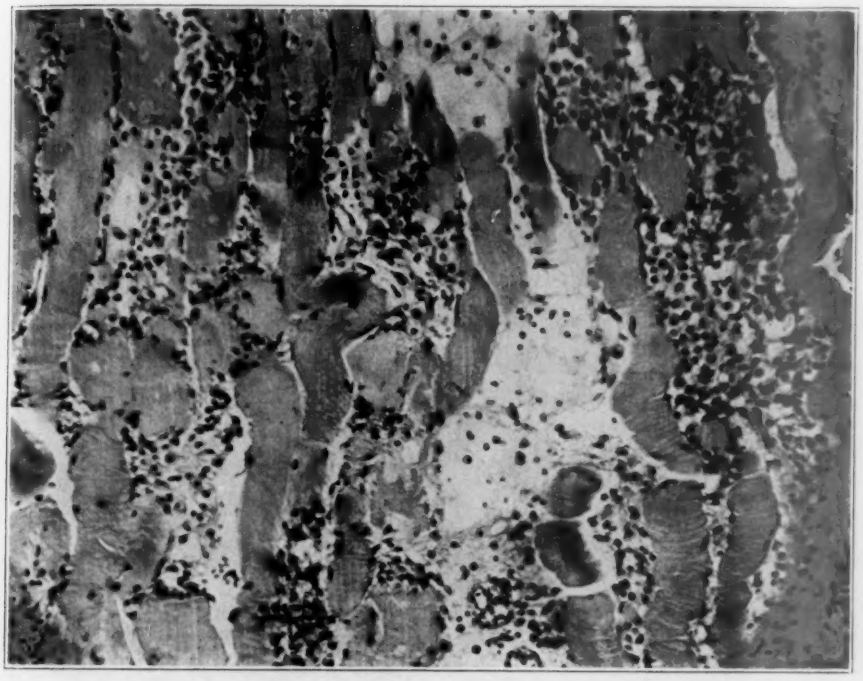

Fig. 2 (case 1).—High power view of a section of striated muscle showing swelling, irregularity and poor striation of the fibers and round cell infiltration.

diastolic murmur at the apex. The liver and spleen were not enlarged, and there was no glandular swelling. The superficial reflexes could not be obtained; the urine was normal and the blood count was normal except for 5 per cent eosinophils. A diagnosis of dermatomyositis was suggested as the only possibility that might explain the entire clinical picture and history. The patient was admitted to Mount Sinai Hospital on Jan. 9, 1930, about the beginning of the sixth month of her illness. The findings were essentially the same as described, except that the edema was less marked, some of the cutaneous lesions had improved, and the child could move her toes and fingers. Ulcerations in the inguinal folds and over the internal maleoli had healed, leaving punched-out scars. The temperature was 101.8 F., the pulse rate 120 and respirations 28. From that time until death, there were fluctua-

tion of the edema and intensity of the skin eruption. A fine purpura appeared on both ankles, telangiectatic lesions were found on the knuckles and face, the skin became shiny and atrophic, and the pigmentation of the forehead cleared up partly. The child gradually was able to move her arms enough to feed herself, and when propped up in a sitting position could bend her knees but not abduct or rotate her thighs. She could lift her head and turn it from side to side. The temperature dropped to normal, but fever recurred off and on for one or more days.

A biopsy of the biceps muscle performed on January 16 showed the typical picture of dermatomyositis: atrophy of the skin, edema and fragmentation of the muscle fibers, loss of striation, fatty degeneration, round cell infiltration and perivascular infiltration around the small vessels.

Fig. 3 (case 1).—Section showing the same conditions as figure 2, plus involvement of the blood vessel wall, perivascular infiltration of round cells and leukocytes and separation of the muscle fibers by edema.

The following laboratory tests were done and the following results were obtained: Wassermann test of the blood, negative; hemoglobin, 72 per cent; white blood cells, 4,700, with 67 per cent polymorphonuclears, 4 per cent mononuclears, 20 per cent small lymphocytes and 9 per cent eosinophils; blood urea, serum, 13 mg. per hundred cubic centimeters; cholesterol, 200 mg.; calcium, 12.4 mg.; phosphorus, serum, 5.8 mg.; albumin, 5.03 per cent; globulin, 2.6 per cent total protein, 7.64 per cent; total fat, 1,200 mg.; blood pressure, 114 systolic and 70 diastolic. The sugar tolerance before the ingestion of dextrose was 75 mg. per hundred cubic centimeters; after forty-five minutes it was 175 mg.; after one hour and forty-five minutes, 160 mg.; after two hours and thirty minutes, 110 mg., and after three hours, 90 mg.

The urine was found to be normal on repeated tests, and the stool was negative for ova and parasites. The Pirquet test was negative and the Mantoux test was negative from 1 to 10 mg. The Schick test was negative; the electrocardiograph was negative. The roentgenograms of the heart, lungs and sinuses were negative. The electrical reactions of the muscles were normal, the cathodal closure contraction being greater than the anodal; there was prompt response to the faradic current. The capillaries of the nail beds were normal. Examination of the nose and throat gave negative results. Dermatologists concurred in the diagnosis of dermatomyositis. A blood culture just before death was positive for Streptococcus hemolyticus. Earlier in the patient's illness the blood culture was sterile.

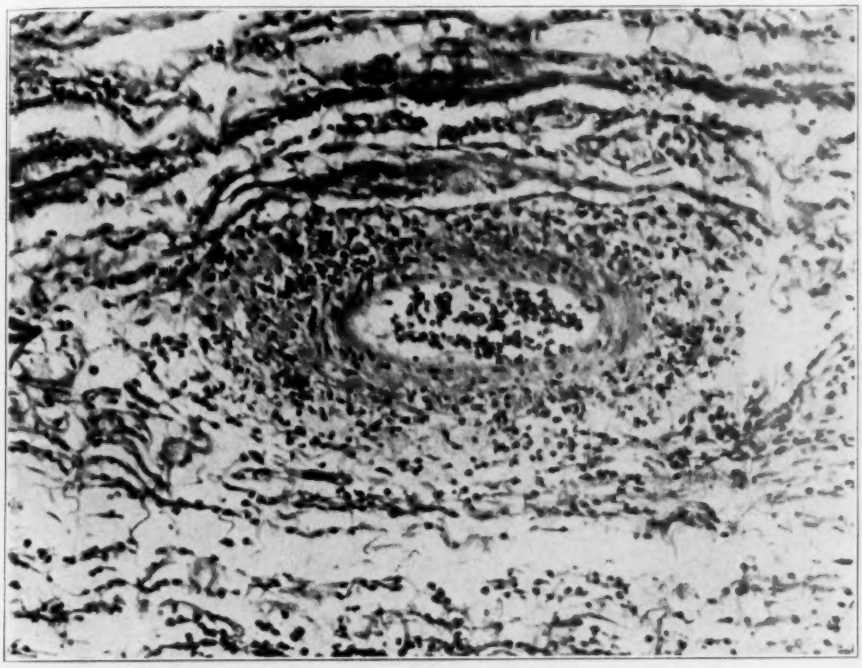

Fig. 4 (case 1).—Section through small intestine showing marked edema and round cell infiltration between the fibers of the muscular layer.

The child had varied treatment. A transfusion of 300 cc. of blood seemed to cause no change in her condition. Potassium iodide, 3 minims (0.18 cc.) given three times a day for more than two months seemed to produce no effect. Exposure to infra-red and ultraviolet rays and to massage at times caused exacerbation of fever. A special diet rich in carbohydrate and low in fat was given for two months. Colonic irrigations were also given daily for over two months, with questionable results. A sharp rise in temperature followed the removal of a piece of muscle for biopsy, suggesting the infectious nature of the disease. Several decubitus ulcers developed on the back, and some ulcerations in the axillae. These lesions did not heal under the usual treatment, and the patient died with a terminal bacteremia and a temperature of 106.5 F., which seemed to originate in one of the ulcers on the back.

Review of Cases from Literature

Author	Date	Age, Years	Sex	Onset	Fever	Skin Changes	Parts of Body Involved	Duration	Outcome	Comment
Fuckel: Cor. Bl. d. allg. ärztl. Ver. v. Thüringen, 1892, vol. 74	1892	8	F	Diarrhea and fever	Yes	Erythema; urticaria	Arms and legs	8 days	Died	Muscle removed; post-mortem examination showed typical changes
Janicke: Deutsche med. Wehnschr. **21** :117, 1895	1895	3	F	.....	....	None	Neck and later entire body	4 months	Recovered	Muscle weakness lasted three months
Koster [28]	....	8	M	Sore throat; fever; vomiting; constipation; pain in legs; inability to walk	Yes	Purpura after three weeks	Extremities	.....	Recovered	Hemorrhagic nephritis in fourth week of illness; recovery was complete
Oppenheim (footnote 9, second reference)	1899	8	M	Pain in neck; inability to walk	....	Erythema on face and eyelids; atrophic scars; oral mucous membranes involved	Entire body	.....	Survived	Reflexes normal; electrical reaction normal; four years later thought to be case of scleroderma
Schultze: Deutsche Ztschr. f. Nervenh. **6** : 245, 1894-1895	....	3	M	Muscular pain; inability to walk	Yes	Scaly eczema after six months	Entire body	21 months	Survived	Eczema healed, muscle atrophy and contracture remained
Cassirer [29]	1898	8	F	After acute infection; transient paresis of extremities	....	.....	Entire body	.....	Survived	Electrical reactions diminished; muscle atrophy
Schuller [24]	1903	7	M	After pertussis, G. I. symptoms; temperature 39 C. (102.2 F.); pain in face and neck; edema of entire body	Yes	Flighty exanthem of chest at onset	Entire body	15 months	Survived	Onset: abdominal pain, diarrhea, edema and temperature 39 C. (102.2 F.); roentgen examination of muscle suggested; trichina plaques; recovery was complete; no eosinophilia
Christen: Cor.-bl. f. schweiz. Aerztl **23** : 822, 1903	1903	10	M	Rheumatoid pains	Yes	Pemphigus-like eruption	Face, abdomen, arms, legs	5 weeks	Recovered	Had had tuberculous knee and epidydimitis, several years before

Batten [19]	1912	9	F	Posttonsillectomy	Yes	.....	Entire body	15 months	Died	Illness followed tonsillectomy; autopsy showed usual and vascular changes
Bruns, Cramer and Ziehen: Handbuch Nervenkrankheiten im Kindesalter, Berlin, S. Karger, 1912, p. 53	1912	14	F	.....	....	Cutaneous hemorrhages	.....	.....	Survived	
Comby: Arch. de méd. d. enf. 1: 923, 1912	1912	9	F	Pain; edema; rash on face	Yes	Erythema of face	Entire body	5 months	Died	Salicylates, iodides, mercury, fibrolysin and physical therapy used
Thursfield [30]	1920	6	M	Walking on toes; red patches on back of neck	....	Scleredema	Lower extremities and back	More than a year	?	Diagnosis between scleroderma and dermatomyositis
Heckscher (footnote 30, first reference)	1925	7	M	Fever; pain in right side of body	Yes	Thickening	Right side of body	.....	Recovered	
Lehmkuhl: Arch f. Kinderh. 86: 179, 1924	1928	8?	F	Muscular weakness	Yes	Edema; eruption	Entire body	6 months	Died	Pneumonia
Moore and Koch [16]	1928	5	M	Fever and extreme weakness	Yes	Bronzing of arms	Entire body	3 months	Died	Terminal sepsis; Staphylococcus aureus; autopsy revealed cellulitis neck and pyuria, latter from onset
Steiner (footnote 7, second reference)	1922	3	F	Soreness of body	Yes	Eyelids red; circumoral dermatitis	Entire body	3 months	Died	Pneumonia; heart muscle involved
Potain (footnote 33, first reference)	1875	17	M	Malaise; pain in extremitis; eyelids red	Yes	Erythema	Pharynx and extremities	6 months	Died, autopsy	Pneumonia
Heckscher [31]	1925	18	M	Muscular weakness and fever	Yes	Papulonodular and later petechial lesions	Entire body	.....	Died, autopsy	Infarcts of lung; myositis; myocarditis; hemorrhages
Kakels [32]	....	..	..	.....	....	.....	.....	.....	.....	Localized areas of calcification in muscles of extremities

The postmortem diagnosis was dermatomyositis, acute sepsis, enterocolitis, decubitus ulcers, hypostatic congestion of the lungs, fatty degeneration of the liver and parenchymatous degeneration of the liver, spleen and heart. Two striking features in the pathologic condition were the involvement of the musculature of the blood vessels and the intestinal ulceration. Although involvement of the mucous membrane has been reported, no mention of intestinal lesions of this kind was noted heretofore. Batten's case showed similar changes in the blood vessels.

CASE 2.—M. H., a Jewish boy, aged 6 years, whose family and past history are unimportant, was admitted to Mount Sinai Hospital on Aug. 10, 1925, and discharged on Nov. 24, 1925. Four weeks prior to admission he had a mild cold, and one week later complained of sharp, unbearable pain in his thighs, knees, legs, ankles and shoulders. His temperature remained at 103 F. for three days after the pain started. He then became unable to move himself and was unable to sit or stand unsupported and to raise his head. The diagnosis of pes planus, rheumatism and poliomyelitis were suggested. On admission to the hospital he was very weak, afebrile and tender all over. He could not sit or hold his head up; when

Fig. 5 (case 2).—Note the marked and diffuse swelling and the absence of edema of the eyelids. This child lay in the position pictured and was unable to move his extremities or body without pain.

placed in the erect position he walked a few steps but could not turn around. After a few days in the hospital his entire body became markedly edematous. The edema was of a brawny indurated type that did not pit on pressure. His reflexes were sluggish, and the electrical reactions of the muscles showed slow response. Biopsy of the biceps muscle showed marked fragmentation of the muscle fibers, round cell infiltration, edema and loss of striations—typical findings of dermatomyositis. Thyroid in small doses was tried without producing any change. Restriction of fluids, a diet high in protein, the administration of yeast and other methods of therapy were tried, without improvement. Three weeks after admission to the hospital a palatal paralysis developed, and two weeks later aspiration pneumonia and an increase of the generalized edema. Hot packs and heliotherapy seemed to help. Five weeks after admission the patient could sit with support, and after three and a half months in the hospital he was discharged, able to walk with a waddling gait. Subsequent observations showed marked recovery but some residual atrophy and contractures of the muscles.

The following laboratory tests were done: biopsy of the muscle gave the results described. The blood count showed: 14,600 white blood cells, with 70 per cent polymorphonuclears and no eosinophils. The urine was normal. The stools contained no ova or parasites. Chemical examination of the blood showed that it was normal, except for the albumin-globulin ratio (2.63: 3.5); there were 490 mg. of sodium chloride and 10.3 mg. of calcium per hundred cubic centimeters. The roentgenograms of all bones were negative. The electrocardiogram showed a left ventricular preponderance. The blood culture was sterile. The electrical reactions of the muscles were indicative of atrophy. The spinal fluid was normal.

COMMENT

A review of the literature on dermatomyositis in childhood revealed only twenty cases, to which we are now adding two. Of the twenty-two cases, eighteen were accounted for, and seven of these eighteen patients died. The most frequent cause of death was pneumonia, and in the remaining few cases it was terminal sepsis or cardiac involvement.

The diagnoses in several of the cases referred to have been questioned because they were distinguished by a peculiar prominent, atypical symptom or outcome. One of Koster's [28] and one of Cassirer's [29] cases resulted in polymyositis fibrosa; Oppenheim [9] and Thursfield [30] had cases in which the condition might have been scleroderma. Senator [5] reported a case under the title of neuromyositis because neuritic symptoms were prominent. Lepin's case was referred to as one of angiomyositis, because it was thought by Koster that vascular injury was the first phase of this illness. Heckscher's [31] older patient had extensive bleeding, and the case was therefore referred to as one of polymyositis hemorrhagica. In Kakel's [32] case muscle calcification developed, and the condition was considered as polymyositis ossificans. In another of Koster's [28] patients the disease started with sore throat, vomiting, fever and a diffuse purpuric cutaneous eruption, and in the fourth and final week of the illness the condition was complicated by an acute hemorrhagic nephritis. There is a great suspicion that scarlet fever may have played a rôle in this illness, just as it is suggestive that in Potain's [33] case the postmorten observation of endocardial changes and multiple visceral infarcts were evidence of a complicating bacterial endocarditis.

28. Koster: Abortive Dermatomyositis bei einem achtjährigen Knaben, Centralbl. f. inn. Med. **18**:606, 1897.

29. Cassirer: Muskelatrophie an einer Polymyositis, Monatschr. f. Psychiat. u. Neurol., 1898, vols. 3 and 4.

30. Thursfield, K.: Case for Diagnosis, Proc. Roy. Soc. Med. **14**:90, 1921.

31. Heckscher, H.: Zwei Fälle von acuter Myositis, Dermatomyositis, Dermatomyositis hoemorrhagica, Zentralbl. f. d. ges. Kinderh. **18**:569; Ugesk. f. laeger **87**:147, 1925.

32. Kakels, cited by Ibraham, Pfaundler and Schlossman: Handbuch der Kinderheilkunde, Leipzig, F. C. W. Vogel, 1924, vol. 4.

33. Potain: Morve chronique de forme normale, Bull. et mém. Soc. méd. d. hôp. de Paris **12**:1314, 1875; Union méd. de Paris **21**:269, 1876.

It seems evident to us that in all the cases mentioned the condition was polymyositis, but in some a particular symptom was most prominent, while in others emphasis was placed on the final outcome of the disease, for example, fibrosis or calcification of the muscles. It would seem more advisable to refer to all cases of this large group under one name, dermatomyositis, and thus avoid possible confusion.

Unlike the conditions mentioned are the so-called specific myosites due to syphilis, trichinosis, avitaminosis or ergot poisoning. In each of these a definite etiology is known, and treatment is usually successful.

It is more difficult to decide in what category to place acute fulminating pyogenic polymyositis. Unlike dermatomyositis, this condition has a rapidly fatal outcome, and in every case abscesses of the muscles and bacteria, usually streptococci or staphylococci, are found. Steiner and others did not regard the condition as being the same as dermatomyositis. Fraenkel [34] and others and recently Bass and Denzer [35] have reported such cases and suggested the possibility of this disease being the extremely acute type of the same condition that in the more chronic form is represented by dermatomyositis. Although we are inclined to believe that acute fulminating myositis is a different disease, since in no case of dermatomyositis, even the rapidly fatal ones, has the infectious agent been found, we cannot deny the possibility of the theory stated by Bass and Denzer.

In making the diagnosis of dermatomyositis it is often necessary to rule out trichinosis, acute rheumatic fever, avitaminosis, scleroderma, poliomyolitis in its early stages, and polyneuritis. It seems unnecessary to go into the differential diagnosis, since the paragraphs on the symptomatology and the course of the illness, all of which were so typically represented in case 1, offer adequate diagnostic aids. Withal it is often impossible to be sure of the diagnosis without a biopsy of the muscles or therapeutic tests.

The etiology of the disease is still obscure, but we believe that it is bacterial or due to bacterial toxins. Blood and tissue cultures were negative in our cases, except one blood culture taken just before the patient in case 1 died, which contained a streptococcus. An observation that favors the infectious nature of the disease is the rise in temperature that followed the removal of a piece of muscle for biopsy and occurred after massage was given during the acute stage of the disease in both of our cases. Unless an infection or toxin was stirred up, we are at a loss to explain this observation.

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34. Fraenkel, H.: Deutsche med. Wchnschr. **11**:9110, 1894.

35. Bass, M. H., and Denzer, B.: Polymyositis, Am. J. Dis. Child. **41**:344 (Feb.) 1931.

It is evident from the literature that dermatomyositis has been seen rarely and by few observers. In many instances the person who had seen one case has reported others, which corroborates the statement frequently made by one of us (Dr. Welt) that any one who has ever observed a case of dermatomyositis will surely recognize the next one encountered.

In reporting our two cases we have reviewed the pediatric literature and given a detailed account of the disease in the hope that it may aid in the more frequent recognition of the disease and in the clarification of its etiology.

LIPOID HISTIOCYTOSIS (NIEMANN-PICK TYPE)

SHERL J. WINTER, M.D.
Visiting Pediatrician, St. Elizabeth Hospital
DAYTON, OHIO

The pathology of disturbances of lipoid and fat metabolism is not yet clearly understood. At the present time, a separation of three distinct types, Niemann-Pick, Gaucher and Schüller-Christian, seems justified.[1] In this report, two additional cases of the Niemann-Pick type are presented with comments on their significance in the general problem of this type of disease. The histology has recently been reviewed by Bloom[2] and the chemistry by Sobotka, Epstein and Lichtenstein.[3]

REPORT OF CASES

CASE 1.—*History.*—A white girl, aged 15 months, of gentile parentage, was admitted to St. Elizabeth Hospital on July 20, 1929, with the complaint of loss of weight and irritability. Enlargement of the abdomen had been observed by the mother for the past six months. The patient was the fourth full term child, with a birth weight of 9 pounds (4082.33 Gm.). When the infant was 3 months of age, breast feeding was discontinued because of failure to gain weight. The feeding was changed frequently thereafter, but with little success. The infant had in the past few months become pale and weak and had never been able to sit alone. Recovery was slow after an attack of bronchopneumonia at the age of 8 months. An enlarged spleen was observed at that time. The mother stated that the patient was always nervous and restless and cried frequently as if in pain.

The father and mother and two brothers, aged 3 and 9 years, were living and well. One sister of the patient died at the age of 7 months. Autopsy had not been done, but the hospital record stated that the spleen was enlarged to below the umbilicus, and that there was an enlarged liver, with secondary anemia. The mother stated that the symptoms were similar to those in the present patient. Another sister of this child is the subject of case 2 of this report.

Physical Examination.—The patient was an emaciated white infant with pallor of the skin and mucous membrane. The skin of the hands and feet was scaly. The cervical, inguinal, axillary and epitrochlear lymph nodes were enlarged. The head was normal in shape, but the anterior fontanel was large. A purulent

Submitted for publication, July 7, 1931.
From St. Elizabeth Hospital.

1. Karsner, H. T.: Human Pathology, ed. 3, Philadelphia, J. B. Lippincott Company, 1931.

2. Bloom, W.: Splenomegaly (Type Gaucher) and Lipoid Histiocytosis (Type Niemann-Pick), Am. J. Path. **1**:595, 1925.

3. Sobotka, H.; Epstein, E. Z., and Lichtenstein, L.: The Distribution of Lipoid in a Case of Niemann-Pick Disease Associated with Amaurotic Family Idiocy, Arch. Path. **10**:677 (Nov.) 1930.

material discharged from the right ear. Only four teeth were erupted. The superficial veins on the anterior surface of the chest were dilated. There was some dulness on percussion over the right apex. The heart was normal. The abdomen was enlarged. The spleen extended below the level of the umbilicus and the liver to 3 cm. below the costal margin. There was no apparent abdominal tenderness.

Laboratory Examination.—The blood count showed: red blood cells, 2,000,000; hemoglobin (Dare), 35 per cent; white blood cells, 4,000; polymorphonuclear leukocytes, 56 per cent; large mononuclears, 4 per cent, and small mononuclears, 40 per cent. The red blood cells showed anisocytosis and polychromatophilia; the

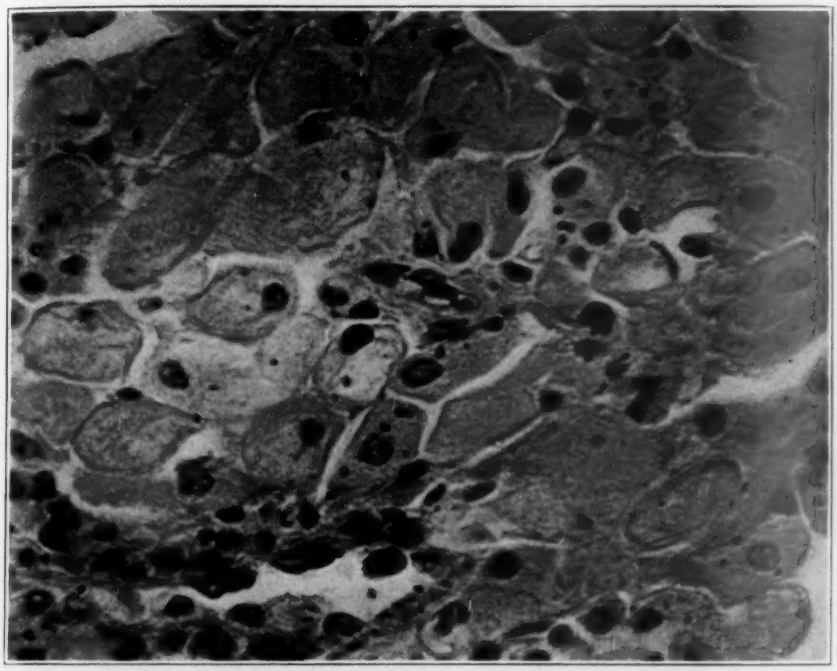

Fig. 1.—Section from the spleen to show the large cells with foamy or granular cytoplasm; × 592.

Wassermann reaction was negative. A roentgenogram of the chest showed some increased density at the apex of the right lung. Intradermal injections of tuberculin in a dilution of 1:1,000 gave negative results.

Clinical Course.—Five roentgen treatments did not produce any notable difference in the size of the spleen. The temperature ranged from 98 to 101 F. Roentgen examination of the chest at the end of the second week showed no change in the area of increased density. Blood examination two weeks after the foregoing report showed: red blood cells, 2,400,000; hemoglobin (Dare), 45 per cent; blood platelets, 150,000. There were present megaloblasts and stippled red cells with anisocytosis and polychromatophilia. Because of the failure of roentgen therapy, splenectomy was done on September 4 after a blood transfusion of 100 cc. The postoperative condition was uneventful until the seventh day, when the incision

opened and was immediately closed with aseptic technic. The blood count on the eighth postoperative day was: red blood cells, 3,600,000; hemoglobin (Dare), 54 per cent, and white blood cells, 9,000. Death occurred on the tenth postoperative day.

The spleen weighed 550 Gm. and measured 15 by 9.5 by 3.5 cm. It was greatly enlarged, with a thick, white, opaque capsule, but without adhesions to the surrounding viscera. It cut with increased resistance, and the substance neither bulged nor retracted from the cut surface. It was firm in consistency and pale gray. The malpighian bodies were not distinct and the entire splenic pulp was of a uniform gray, homogeneous, cellular type. On the anterior surface there was an area 3 cm. in diameter that was yellow and elevated above the surface of the

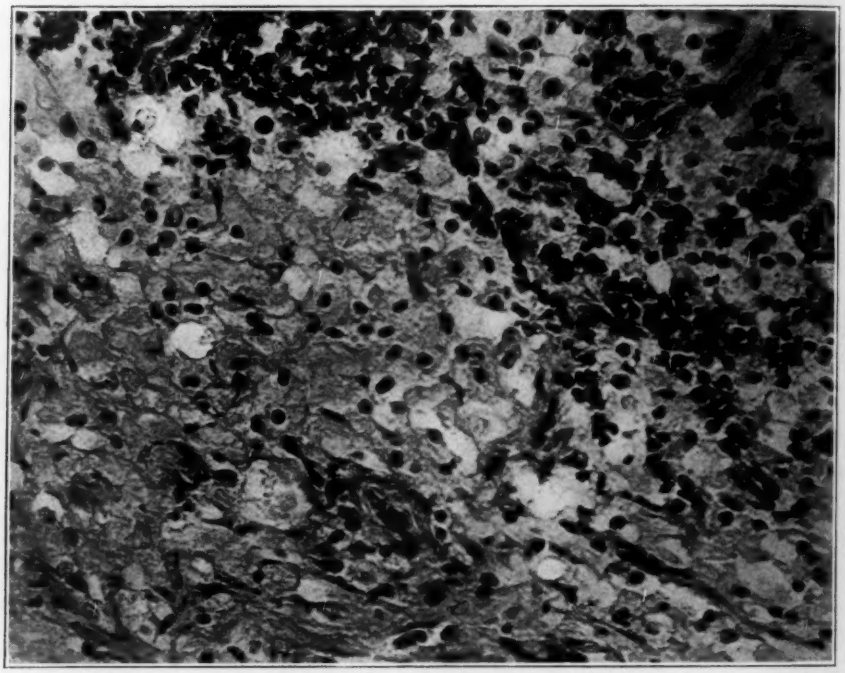

Fig. 2.—Section from bronchial lymph node to show the destruction of architecture and the infiltration with large lipoid-containing cells; × 385.

surrounding spleen. On section, it was found to be pyramidal and extended into the splenic substance for a distance of 3 cm. On microscopic examination, the majority of the splenic pulp was seen to be replaced by the large cells, illustrated in figure 1. These cells varied from 30 to 70 microns in diameter and were polygonal, with a large amount of foamy or granular cytoplasm and a relatively small nucleus, which varied in staining power and contained a prominent nucleolus. The preserved splenic pulp showed no remarkable deviation from normal. Malpighian bodies were small and few. There was no increase of connective tissue, and the trabeculae and blood vessels were normal. The capsule was thickened by an increase of collagenous connective tissue.

Autopsy performed four hours after death revealed lipoid histiocytosis (Niemann-Pick type), conglomerate caseous tuberculosis of the apex of the right lung,

miliary and conglomerate tuberculosis of the tracheobronchial lymph nodes, acute right purulent otitis media and cloudy swelling of the viscera.

The tuberculosis of the apex of the right lung and the miliary and conglomerate tuberculosis of the bronchial lymph nodes were not unusual. The gross description will be limited to the lymph nodes. All lymph nodes, including the retroperitoneal, mesenteric, periaortic and mediastinal, were enlarged and varied from 1 to 3 cm. in diameter. The capsule was not thickened, and all nodes were discrete. They cut with increased resistance and revealed a nonbulging, smooth, homogeneous, gray-yellow cut surface. There was no increase of connective tissue. Microscopically (fig. 2), most of the lymphatic tissue was replaced by the same type of cell described in the spleen. The cells were large, with faceted cell boundaries and a granular or foamy cytoplasm with a small nucleus and a prominent nucleolus. The lymphatic tissue that remained was not remarkable. These same cells were present in the sinusoids of the liver as well as in the spleen and lymph nodes.

CASE 2.—A white girl, aged 4 months, a sister of the patient in case 1, was first seen in February, 1930, because of loss of weight, vomiting and constant crying. Breast feeding was satisfactory for three months, but during the last month the child had refused it frequently, and failed to gain. The mother stated that the patient was very nervous and apparently unable to see.

Physical Examination.—The patient was a fairly well nourished, white infant with poor elasticity of the skin. The fontanels were large, and the superficial veins of the head were distended. The eyes would follow a light to the right, but apparently were unable to observe it past the midline to the left. The eyegrounds were normal. The chest was normal. The abdomen was large, and the spleen was palpable 3 cm. below the costal margin. The liver extended 2 cm. below the right costal border. The reflexes were hyperactive.

Laboratory Examination.—The blood count showed: red blood cells, 4,000,000; hemoglobin (Dare), 80 per cent; white blood cells, 7,600; polymorphonuclear leukocytes, 30 per cent; small mononuclears, 50 per cent; large mononuclears, 10 per cent; blood platelets, 80,000. The intradermal tuberculin test in a dilution of 1:1,000 was negative. Roentgen examination showed a uniform enlargement of the heads of the femurs.

Clinical Course.—The patient was seen regularly over a period of four months. There was increased weakness with loss of weight and failure to take feedings. When she was 6 months of age, a splenic puncture for diagnostic purposes was done. A report on this by Dr. Walter M. Simpson was: "A small tissue fragment from the splenic puncture and a smear showed many large, pale, foamy cells of the type found in Gaucher's disease." Later opisthotonos and marked hypertonicity developed. The temperature ranged from 100 to 103 F. Death occurred at 8 months of age. Autopsy was not permitted.

COMMENT

Although the chemical examinations described by Sobotka, Epstein and Lichtenstein [3] were not carried out in case 1, there is little doubt from the standpoint of histopathology that this case is one of lipoid histiocytosis of the Niemann-Pick type. In case 2 the result of the splenic puncture revealed that the disease was also of the lipoid histiocytosis group, but a definite diagnosis could not be made. In the case of the other sister who died at an earlier age no diagnosis is

possible, but it would be reasonable to assume from the story given by the mother that a similar type of disease may have been present.

The cases here reported are essentially typical of the disease, with the exception that leukopenia was observed in both cases, although this is not the first report of such an occurrence. Another point of interest is the presence of meningeal symptoms late in the course of the disease in case *2*, as was previously reported by Stransky.[4]

The familial incidence of the Niemann-Pick type of lipoid histiocytosis has been observed by Bloom [2] and others.

Harris Building.

4. Stransky, E.: Ueber grotzzellige Splenohepatomegalie, Jahrb. f. Kinderh. **126**:204, 1930.

FAMILIAL JUVENILE CIRRHOSIS OF THE LIVER

MORRIS L. BRIDGEMAN, M.D.
AND
THOMAS D. ROBERTSON, M.D.
PORTLAND, ORE.

Cirrhosis of the liver, especially the atrophic type, is a rare disease in children, and for this reason is of sufficient interest to justify reports. Sutton,[1] in 1930, recorded the thirteenth case of nonalcoholic primary atrophic cirrhosis of the liver in a child. It has been estimated by Morse[2] that one of every 20,000 children may have one of the various types of cirrhosis. However, autopsy statistics on this same number might reveal a higher incidence.

The same forms of cirrhosis that one finds in adults are noted in juveniles, with the addition of a few that are peculiar to children and infants alone. The majority of the cases quoted in the literature have been multilobular, biliary obstructive or syphilitic in nature. The first type, multilobular or alcoholic cirrhosis, is noted more often among foreign children, and is thought to be the result of the early use of alcoholic beverages by such children. Jones[3] collected seventy-two cases in 1907, and added two of his own. Elterich,[4] Ely,[5] Blakely,[6] Still[7] and others have contributed to the reports on this type of cirrhosis. Syphilitic and biliary cirrhosis predominate in the cases reported. Babboneix and Paisseau,[8] Weil,[9] Joukovsky[10] and many others have written on syphilitic cirrhosis of childhood.

Submitted for publication, July 19, 1931.

From the Departments of Pediatrics and Pathology of the University of Oregon Medical School.

1. Sutton, T. L.: Cirrhosis of the Liver in Childhood: Report of a Case of Atrophic Cirrhosis in a Boy Aged Ten Years, Am. J. Dis. Child. **39**:141 (Jan.) 1930.
2. Morse: Boston M. & S. J. **147**:299, 1902.
3. Jones: Brit. J. Child. Dis. **4**:1, 1907.
4. Elterich: M. & J. Rec. **126**:293 (Sept.) 1927.
5. Ely: Boston M. & S. J. **170**:542 (April 2) 1914.
6. Blakely: Boston M. & S. J. **162**:245 (Feb. 24) 1910.
7. Still: Common Disorders of Childhood, ed. 3, Oxford Medical Publication, New York, Oxford University Press, 1920, p. 310.
8. Babboneix and Paisseau: Bull. et mém. Soc. anat. de Paris **84**:442 (July) 1900.
9. Weil: Lyon méd. **115**:1108 (Dec. 25) 1910.
10. Joukovsky: Syphilitic Cirrhosis of the Liver in an Infant, Am. J. Dis. Child. **33**:904 (June) 1927.

Another group of cirrhosis present in children is found in India and in some parts of Mexico. This has been studied by Gibbons,[11] Mackenzie,[12] Pearse [13] and Ghose,[14] who have noted a marked familial tendency in this type of pathologic process, somewhat the same as that found in Hanot's cirrhosis.

Congestive cirrhosis, as described by Hutnell,[15] Hanot [16] and Parmentier [17] under cardiac cirrhosis (cirrhose cardiaque), is found in children having chronic passive congestion associated with heart disease. The familial tendency of the cirrhosis has been described in many of its various forms, but has been especially noted in the Indian or tropical type and in Wilson's [18] disease.

Gunn [19] reported the case of a 4 year old girl, who had lost weight since she was 3 years of age, with progressive enlargement of the abdomen. Necropsy revealed atrophic cirrhosis of the liver, cirrhosis of the pancreas and histologic changes in the spleen of the nature of a diffuse fibrosis and fibro-adenitis of the follicles. A brother of this child had exhibited similar signs, and had died at the same age three years previously. This girl was considered to have a splenomegalic cirrhosis. In this group are included those cases in which the prominent features are first the enlargement of the spleen, with the liver involvement becoming manifest toward the end of the illness. These cases at the start are usually designated as splenic anemia or Banti's disease. The case reported in this paper is very similar to the one reported by Gunn, and we believe should come under the classification of splenomegalic cirrhosis or familial juvenile cirrhosis of the liver.

The term familial juvenile cirrhosis of the liver is given to a syndrome such as is presented in the case reported here because of the lack of a better understanding of the etiology and pathogenesis of such conditions. MacMahon, Lawrence and Maddock [20] produced obstructive cirrhosis in guinea-pigs by ligating the common bile duct, with subsequent fibrosis limited to the perilobular regions. MacMahon [21] observed obstructive anomalies of the bile ducts in children and infants,

11. Gibbons: Internat. M. Ann., 1891, cited by Morse (footnote 2).
12. Mackenzie: Lancet **1**:321, 1895.
13. Pearse: Lancet **1**:165 (Jan. 16) 1909.
14. Ghose: Lancet **1**:321, 1895.
15. Hutnell: Boston M. & S. J. **147**:299, 1902.
16. Hanot: Boston M. & S. J. **147**:299, 1902.
17. Parmentier: Boston M. & S. J. **147**:299, 1902.
18. Wilson: Diseases of the Basal Ganglion, in Oxford Medicine, New York, Oxford University Press, 1921.
19. Gunn, F. D.: Familial Juvenile Cirrhosis of the Liver, Arch. Path. & Lab. Med. **1**:527 (April) 1926.
20. MacMahon, Lawrence and Maddock: Am. J. Path. **5**:631 (Nov.) 1929.
21. MacMahon: Am. J. Path. **5**:645 (Nov.) 1929.

producing a perilobular hepatic fibrosis, cirrhosis. He [22] studied seventy-five livers from cases classified as "biliary cirrhosis," as defined by Weber. Five of these were subdivided as uncomplicated infectious cirrhosis, thirteen as combined infectious and obstructive cirrhosis and thirty-nine as uncomplicated obstructive cirrhosis. He presented confirmatory histologic evidence of the purely infectious pathogenesis of the five cases as listed. He also made a pathologic and clinical differentiation between infectious and obstructive cirrhosis.

In infectious cirrhosis there may be clinical evidence of an infectious process with perhaps an initial transient jaundice. In the early stage the liver is normal in size; in the chronic and healing stages it is enlarged, and if there is recovery, the organ may contract to normal size, appearing uniformly nodular. The spleen is enlarged subsequent to portal obstruction from chronic passive congestion and ascites, and dilated collateral veins may be present.

In obstructive cirrhosis there is an initial persistent obstructive jaundice. The liver is normal in size with a smooth capsular surface, except when the obstruction is of long standing. In this condition, the capsule becomes finely granular, simulating Morocco leather. The signs and pathologic evidence of any noteworthy portal obstruction are absent.

In our case no anomalies of the bile ducts or anything that might produce an obstructive jaundice were noted at autopsy. The clinical observations simulate in all respects those of infectious cirrhosis as described by MacMahon and his co-workers. The evidences of portal obstruction, namely, ascites and chronic passive congestive enlargement of the spleen, were present, and pronounced chronic pericholangitis was noted microscopically.

It seems to us that the syndrome manifested in our case fits well into the category of infectious cirrhosis. The evidence of involvement of the liver in other children of the same family may be coincidental in a small percentage of cases and should not of necessity lead to a separate term. Medical philosophers may conjecture on the possibility of a hereditary predisposition that allows organisms to attack the same organ in several children, producing identical pathologic changes of varying degrees.

REPORT OF A CASE

History.—R. A., a boy, was first seen at the age of 6 months. He was brought for examination because he was not progressing well, did not eat unless forced, and because his abdomen was very large. He was found to be very much undernourished, and the abdomen was greatly distended with gas, which gave the child the appearance of that seen in celiac or Hirshsprung's disease. After the infant was given a high protein diet for a few weeks, an enormous liver was noted to extend below the umbilicus, and at this time a very large spleen was palpated.

22. MacMahon: Am. J. Path. **7**:77 (Jan.) 1931.

The child was given various diets by different doctors and by several charlatans, the parents being willing to try anything. At times the patient would seem to improve, but then intermittent vomiting and abdominal distention would commence. The protein diet seeemed to decrease the gaseous distention somewhat, but, in spite of this, at times the abdomen became enormous, and the size could not be controlled except by the use of enemas and starvation. After various treatments had been tried, the child was seen again at the age of 14 months. He was placed in the Doernbecker Children's Hospital for study. The blood counts, chemical analysis of the blood, Wassermann reaction of the blood and urinalysis showed nothing abnormal. He was discharged after nine days with a diagnosis of undernutrition and enlarged spleen and liver, probably Banti's disease.

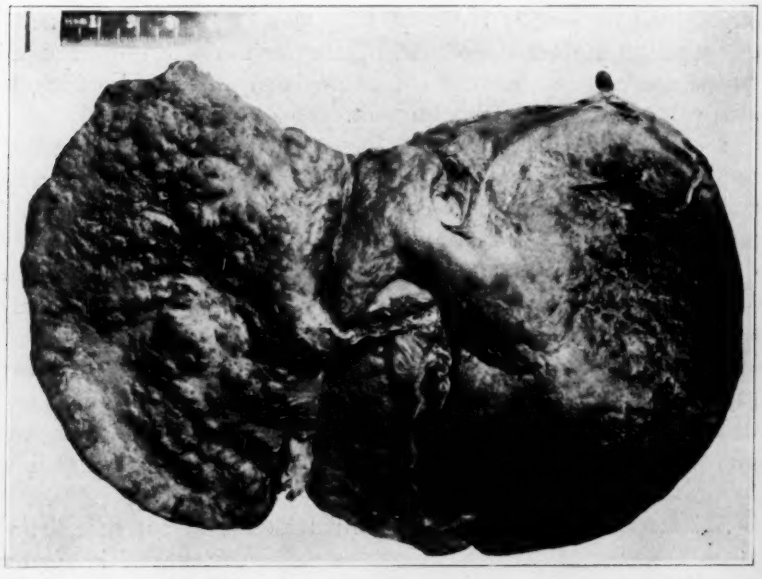

Fig. 1.—Gross photograph of the liver, showing the lobulation visible on the inferior capsular surface. Observe that the lobulation of the left hepatic lobe is more marked than that of the right.

Course.—The patient was brought back one year later, at the age of 26 months, critically ill. His abdomen was huge and contained a large amount of fluid. For the first time he was found to be very jaundiced, and, according to the parents, had been so for two months. After 1,500 cc. of straw-colored fluid was removed from the abdomen, the liver was found to be 2 cm. below the costal border. The red blood cell count was 2,460,000; the hemoglobin, 50.2 per cent (Osgood-Haskins, Sahli), and the differential smear showed no noteworthy change. The fragility test was within normal limits (from 0.48 to 0.34). The patient was again taken home under protest, but returned eight days later in a moribund condition. He was given a transfusion of blood, following which he improved, but was very restless and difficult to keep in bed. He screamed out with a shrill cry like that heard in cases of cerebral disease, but he did not show any of the neurologic findings that would support a diagnosis of Wilson's disease. After three days, his

temperature rose rapidly to 106 F.; he passed into a comatose state and died. Permission was obtained for a postmortem examination of the thoracic and abdominal organs only.

Family History.—Both the mother and father were living and were 35 years of age. They had four children who were older than the patient, aged 16, 8, 6 and 3 years. The 8 year old boy had had a large abdomen until one year ago. An examination of this child revealed the liver to be about two fingerbreadths below the costal border. The 3 year old girl had a distended abdomen, with a liver that was at least two fingerbreadths below the costal border. The mother stated that

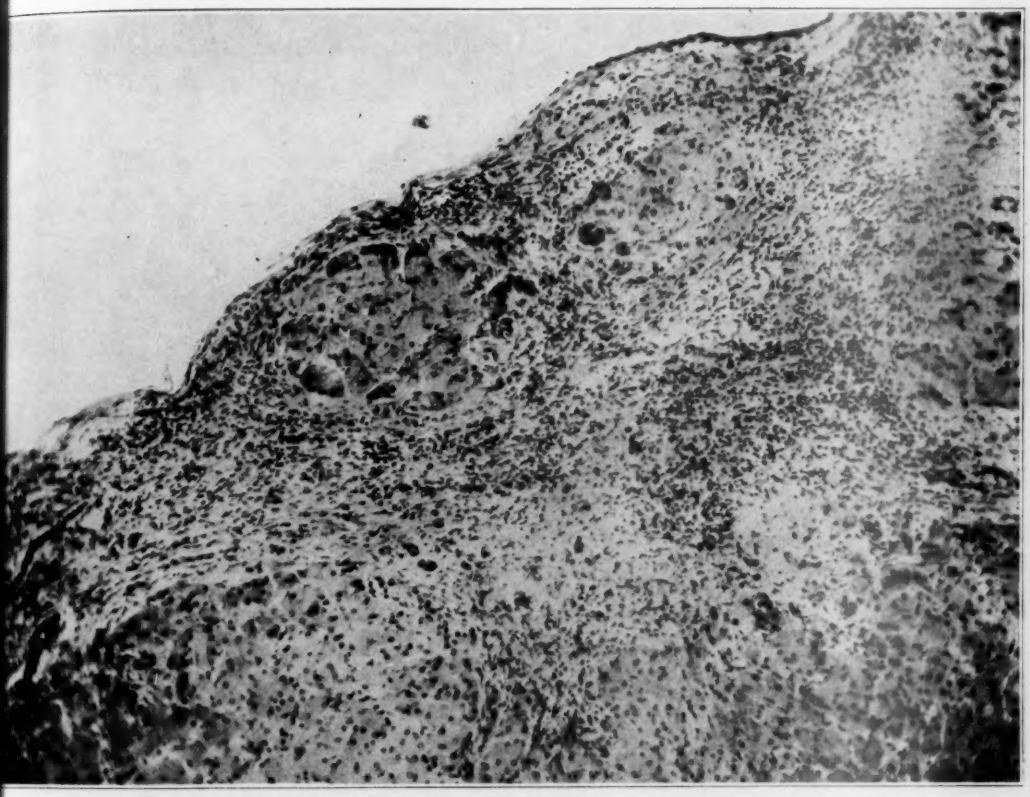

Fig. 2.—Low power photomicrograph, showing the undulating capsular surface and the lobulation due to the fibrosis. Note the diffuse lymphocytic infiltration of the fibrous connective tissue and the branching bile ducts. There is no fibrous invasion of the parenchymal units.

the 8 year old boy had been a difficult child to feed and was very similar to the patient.

The patient had weighed 8 pounds (3,628.7 Gm.) at birth, and seemed to be normal until he was 3 months of age, at which time the abdomen began to enlarge and the vomiting started. He was breast fed until 10 months of age, and the feeding was well regulated except for three months in which his diet consisted mainly of vegetable water. The parents said that they did not use alcohol in any form.

The child had always resided in Oregon. He had had no contagious disease, but had had several infections of the upper respiratory tract, with one attack of acute otitis media. No history of gray stools was obtained, though the parents stated that occasionally the stools were quite tarry.

Autopsy.—External examination disclosed an emaciated child, measuring 80 cm. in length, with a moderate icteric tint of the skin and a few petechial cutaneous hemorrhages over the anterior aspect of the chest and the right forearm. The abdomen was tense and dome-shaped, and a distinct fluid wave was obtained, but no dilated superficial abdominal veins or caput medusae were noted.

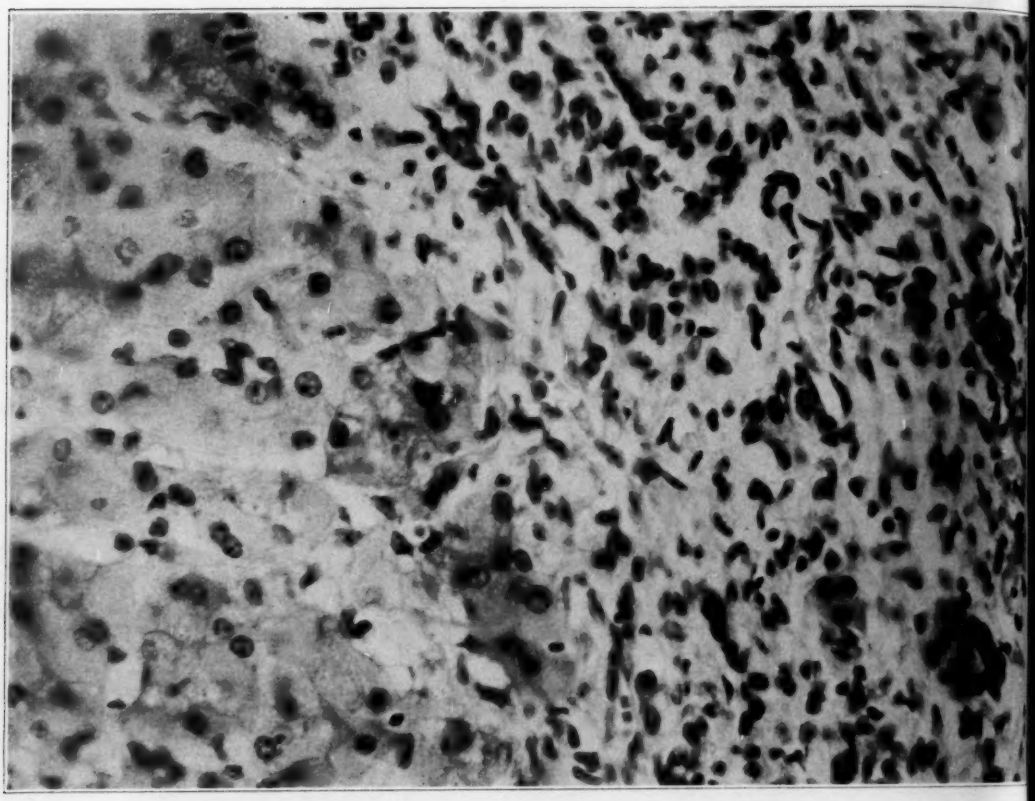

Fig. 3.—High power photomicrograph of the liver, demonstrating hypertrophy of the hepatic cells, lymphocytic infiltration of the connective tissue (pericholangitis), proliferating bile ducts and limitation of the fibrosis to a perilobular distribution.

The abdomen contained 800 cc. of clear straw-colored fluid devoid of fibrin, and the mesenteric veins were slightly engorged, with no apparent dilated veins of a collateral venous return. The spleen, weighing 350 Gm. and measuring 13 by 8 by 6.5 cm., was free from adhesions, exhibiting a tense, smooth, purplish capsule. The inferior pole reached 9 cm. inferior to the left costal margin. The cut surfaces were fairly firm and a deep purplish red, with the reticulated stroma apparently not increased and on the same level as the parenchyma. The malpighian corpuscles

were grossly indistinct. The liver extended just beyond the right costal margin, presenting a blunt, finely nodular inferior margin. The weight of this organ was found to be 550 Gm. and the diameters 17 by 11 by 7 cm., with the greatest diameter the transverse. The ventral dorsal capsular surface was flatly nodular, while the nodularity was more pronounced on the inferior aspect, being especially marked over the left lobe, as shown in figure 1. The cut surfaces were very firm and yellow, and presented a finely lobulated appearance, with varying-sized small yellow lobules separated by depressed, whitish, firmer, narrow strands of fibrous stroma. The hepatic tissue cut with greatly increased resistance. The biliary lymph nodes were considerably enlarged, with the cut surfaces presenting the appearance of pale yellow, bile-stained lymphoid tissue and a distinctly discernible central softer medulla and a paler and firmer peripheral cortex. The gallbladder and bile ducts presented no gross evidence of fibrosis or of active inflammation, and no adhesions were noted in this region. The bile ducts were all patent and of normal caliber, with no anomalies of the gallbladder. The ampulla of Vater and its ostium were easily opened. Numerous small petechial hemorrhages of the gastric mucosa were apparent. The right side of the heart was dilated, and the endocardium and intimal surface of all of the blood vessels were stained pale yellow with bile pigment. A few small transverse atheromatous plaques were noted on the intimal surface of the ascending aorta, limited to the superior margins of the sinuses of Valsalva, with none observed in any other portion of the aorta. Areas of bright red recent hemorrhage mottled the lung and right suprarenal gland. The parenchymatous organs were pale, concomitant with the secondary anemia present.

Microscopic sections from different parts of the liver disclosed spheroidal lobules of hepatic cells of varying sizes separated by fibrous connective tissue bands, some thicker than others. None of the many sections showed fibrous invasion of the lobules, and the hepatic cells at the periphery of each were more compactly arranged than those more centrally placed. The venous sinuses were somewhat narrowed and contained slightly less blood than is normally found. The hepatic parenchymal cells were large, with slight hyperchromatism of the nuclei, and in the cytoplasm of some, finely amorphous bile pigment was noted. In occasional lobules parenchymal cells showed a vacuolated cytoplasm with pyknotic nuclei, and a few contained single and multiple fat globules of various sizes. A diffuse moderate lymphocytic infiltration of the fibrous stroma was uniformly present, but no plasma cells or epithelioid cells were found to suggest an active syphilitic inflammatory process. Branching, collapsed, proliferating bile ducts were found in all parts of the thickened connective tissue trabeculae.

Microscopic sections of the spleen revealed splenic sinusoids distended with blood. Large phagocytic cells heavily laden with hemosiderin were numerous and uniformly present in all sections. A relative decrease in the lymphocytes was noted with no apparent increase in the reticulum and no fibrosis.

CONCLUSIONS

1. The fourteenth case of atrophic cirrhosis of the liver in children is reported.
2. Evidence of a familial tendency is noted in this case.
3. The possibility of an infectious etiology is considered.

Progress in Pediatrics

THE WEIGHT OF THE THYMUS GLAND IN HEALTH AND IN DISEASE

EDITH BOYD, M.D.
MINNEAPOLIS

In spite of the repeated demonstration that the thymuses of healthy, well nourished children are prominent and average 20 Gm. or more in weight and that wide thymic shadows on roentgenograms of infants' chests are common, the belief persists that these findings represent a constitutional susceptibility to death from trivial causes, i. e., status thymicolymphaticus, and account for most respiratory symptoms of infancy. Because of the tenacity of these misconceptions, I have undertaken to demonstrate their fallaciousness first by a review of the normal growth phenomena of the thymus and of its reaction to disease and inanition, second by a graphic presentation of these phenomena from additional data, and third by a comparison of the statistics from the new data with those obtained by previous workers.

INVOLUTION AND GROWTH PHENOMENA

According to Jackson,[1] various earlier workers recognized that the thymus and lymphoid tissue, like other organs, atrophied with inanition. Since the thymus appeared to respond more quickly than other organs to disturbances of nutrition, Simon [2] in 1845 called it "a barometer of nutrition and a very delicate one." However, most of the older medical works indicate a long association of a prominent or "enlarged" thymus with sudden death in infancy.[3] In 1858, Friedleben [4] denied the existence of this association, and since then the dis-

From the Institute of Child Welfare and Department of Anatomy, University of Minnesota.

1. Jackson, C. M.: The Effects of Inanition and Malnutrition upon Growth and Structure, Philadelphia, P. Blakiston's Son & Co., 1925, p. 285; Recent Work on the Effects of Inanition and of Malnutrition on Growth and Structure, Arch. Path. **7**:1042 (June) 1929; **8**:81 (July); 273 (Aug.) 1929.

2. Simon, J.: A Physiological Essay on the Thymus Gland, London, H. Renshaw, 1845; quoted by Jackson (footnote 1).

3. According to J. Ruhräh (Pediatrics of the Past, ed. 1, New York, Paul B. Hoeber, Inc., 1925, p. 239), Felix Plater in 1614 first ascribed death to suffocation by an enlarged thymus.

4. Friedleben, A.: Die Physiologie der Thymusdrüse im Gesundheit und Krankheit, Monograph, Frankfurt-am-Main, 1858.

cussion has continued unabated as to the exact rôle the thymus plays in sudden and unexpected deaths. In the earlier literature death was considered to be due to pressure of the "enlarged" thymus on the trachea or other adjacent vital organs. Gradually the concept arose that this pressure also caused most respiratory symptoms in infancy, and recently even gastro-intestinal symptoms. These are loosely called "thymic symptoms" or the "thymic syndrome." [5]

In 1889 and 1890, Paltauf [6] advanced the theory that the prominent lymphoid tissue and thymus found in children and in young adults dying suddenly of no demonstrable cause represented an abnormal constitutional state in which the person was highly susceptible to death from trivial causes. This supposedly abnormal condition became known as the lymphatic constitution, lymphatic state and status thymicolymphaticus. Many secondary signs and symptoms have been associated with it,[5] but only two characteristics are consistently reported, namely, prominent or so-called "enlarged" thymus and lymphoid tissue and death or liability to death from trivial causes. Any thymus weighing 20 Gm. or more is considered "enlarged."

With the recognition of the nature of the function of ductless glands, either an abnormal or excessive secretion or an imbalance between the secretion of the thymus and other ductless glands [7] has been considered the cause of status thymicolymphaticus.

At the end of the last century the discovery of the roentgen ray introduced technics both for estimating the size of the thymus before death and for reducing its size. The association of "thymic symptoms" and a prominent thymus could be verified in the living patient, and the wide shadow could be reduced by irradiation. By this time the concepts that a prominent thymus produced symptoms by direct pressure and that it was a sign of the lymphatic state were inextricably intermingled. Hence reduction of the thymus by irradiation was supposed both to relieve "thymic symptoms" and to destroy the liability to sudden death.[5] The situation has come to such a pass that the surgeon who does not have the child with a wide shadow treated by irradiation before the administration of an anesthetic may be held liable for malpractice if the child dies while under anesthesia.

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5. For a summary of symptoms and references see Boyd, E.: Growth of the Thymus: Its Relation to Status Thymicolymphaticus and Thymic Symptoms, Am. J. Dis. Child. **33**:867 (June) 1927; Growth and Development of the Thymus, Committee on Growth and Development, White House Conference Report, to be published; abstr., Am. J. Dis. Child. **42**:205 (July) 1931.

6. Paltauf, A.: Ueber die Beziehung der Thymus zum plötzlichen Tod, Wien. klin. Wchnschr. **2**:877, 1889; **3**:172, 1890.

7. Marine, D.: Status Lymphaticus, Arch. Path. **5**:661 (April) 1928.

Since Friedleben's time a few voices have been raised persistently in opposition to these concepts. Foremost among these has been that of Hammar. He has established the normal growth phenomena of the thymus, both gross and microscopic, described its reaction to disease and critically annotated the voluminous literature in his "Fifty Years of Thymus Investigations," [8] published in 1910, and "The Human Thymus in Health and Disease," [9] published in 1926 and 1929. As early as 1906, Hammar [10] found that the thymus of healthy persons dying of accidental causes within twenty-four hours of the injury weighed as much as those from persons dying of "status thymicolymphaticus." He demonstrated that the thymus from healthy persons killed by accident has an average weight of approximately 12 Gm. at birth, 25 Gm. by 3 years, 30 Gm. by puberty and 15 Gm. by senility.

Using similar criteria for selecting normal subjects, von Sury,[11] Bratton,[12] Boyd,[5] Greenwood and Woods,[13] the Status Lymphaticus Investigation Committee as reported by Stewart,[14] and Young and Turnbull [15] have confirmed Hammar's results for the postnatal period. Moreover, Scammon [16] graphically demonstrated that although Ronconi's [17]

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8. Hammar, J. A.: Fünfzig Jahre Thymusforschung, Ergebn. d. Anat. u. Entwcklngsgesch. **19**:1, 1909.

9. Hammar, J. A.: Die Menschenthymus in Gesundheit und Krankheit: I. Das normale Organ, Ztschr. f. mikr.-anat. Forsch., 1926, supp. vol. 6; II. Das Organ unter anormalen Körperverhältnissen, ibid., 1929, supp. vol. 16.

10. Hammar, J. A.: Ueber Gewicht, Involution und Persistenz der Thymus im Postfötalleben des Menschen, Arch. f. Anat. u. Entwcklngsgesch., supp., 1906, p. 91.

11. von Sury, K.: Ueber die fraglichen Beziehungen der sogenannten Mors thymica zu den plötzlichen Todesfällen im Kindesalter, Vrtljsschr. f. gerichtl. Med. **36**:88, 1908.

12. Bratton, A. B.: The Normal Weight of the Human Thymus, J. Path. & Bact. **28**:609, 1925.

13. Greenwood, M., and Woods, H. M.: "Status Thymico-Lymphaticus" Considered in the Light of Recent Work on the Thymus, J. Hyg. **26**:305, 1927. Greenwood, M.: A Further Note on "Status Thymico-Lymphaticus," ibid. **30**:403, 1930.

14. Stewart, M. J.: Status Lymphaticus, Interim Report of the Committee Appointed Jointly with the Medical Research Council, J. Path. & Bact. **28**:132, 1925.

15. Young, M., and Turnbull, H. M.: An Analysis of the Data Collected by the Status Lymphaticus Investigation Committee, J. Path. & Bact. **34**:213, 1931.

16. Scammon, R. E.: A Summary of the Anatomy of the Infant and Child, in Abt, I. A.: Pediatrics, Philadelphia, W. B. Saunders Company, 1923, vol. 1, p. 257.

17. Ronconi, T. L.: Comportamento del timo dell'uomo nelle varie età della vita e in svariate condizioni morbose, Mem. d. r. Accad. d. sc. di Modena, 1909, series 3, vol. 9; Path. Riv. quindicin., Genova **1**:565, 1908-1909.

mean weights for Italian data are consistently less, they form the same curve with age as Hammar's.[10]

In the fetal period the thymus increases from about 1 mg. at 3 lunar months to 10 Gm. at 10 lunar months.[9] Also, Scammon [18] found that the weight of the thymus has a closer relation to body weight than to body length, and it increases at a faster rate than the body weight.

With birth two changes take place in the thymus. First the gland is compressed from a broad to a narrow elongated form by the expanding lungs, and second it temporarily decreases in weight. The latter change was noted by Gräper [19] and myself.[20] The former change has been demonstrated from anatomic dissection by Gräper [19] and Noback [21] and from roentgenograms by Wasson [22] and Shannon.[23]

Moreover, like Hammar and Friedleben before him, all these workers have recognized the high variability of the weights of the glands even in carefully selected subjects. Scammon [16] aptly stated that the normal high variability makes it "extremely difficult to draw a sharp line between the normal and abnormal cases on the basis of weight alone."

Also, Vierordt,[24] Legou,[25] Hammar,[10] Jackson,[26] Hoskins [27] and Young and Turnbull [15] demonstrated by percentage ratios of thymus weight to body weight that the relative amount of thymus and lymphoid tissue increases in fetal life until birth, and then decreases throughout

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18. Scammon, R. E.: The Prenatal Growth of the Human Thymus, Proc. Soc. Exper. Biol. & Med. **24**:906, 1927.

19. Gräper, L.: Die anatomischen Veränderungen kurz nach der Geburt, Anat. Hefte **59**:45, 1920; Brustorgane des Kindes, in Peter, K.; Wetzel, G., and Heiderich, F.: Handbuch der Anatomie des Kindes, Munich, J. F. Bergmann, 1928, vol. 1, p. 293.

20. Boyd, E.: Neonatal Decrease and Recovery in Thymus Weight of Man, Anat. Rec. **45**:207, 1930; footnote 5.

21. Noback, G. J.: A Contribution to the Topographic Anatomy of the Thymus Gland, with Particular Reference to Its Changes at Birth and in the Period of the New-Born, Am. J. Dis. Child. **22**:120 (Aug.) 1921.

22. Wasson, W. W.: The Thymus Gland, Arch. Otolaryng. **4**:495 (Dec.) 1926; Radiography of the Infant Chest, Radiology **5**:365, 1925.

23. Shannon, E. H.: Some Observations on the Thymus in Early Infancy, Canad. M. A. J. **22**:775, 1930.

24. Vierordt, H.: Anatomische, physiologische und physikalische Daten und Tabellen, ed. 3, Jena, Gustav Fischer, 1906, p. 44.

25. Legou, E.: Quelques considérations sur le développement du foetus, Thèse de Paris, 1903; quoted by Scammon (footnote 18).

26. Jackson, C. M.: On the Prenatal Growth of the Human Body and the Relative Growth of the Various Organs and Parts, Am. J. Anat. **9**:119, 1909.

27. Hoskins, E. R.: Is There a Thymic Hormone? Endocrinology **2**:241, 1919.

postnatal life. As a result the normal thymus decreases in prominence in the postnatal period even though it actually increases in size until puberty. This is clearly illustrated by considering that the body doubles its birth weight by 6 months, triples it by 1 year and has increased tenfold by 10 years, while the thymus doubles its birth weight by 6 months, triples it by 6 years and thereafter increases only a few grams in average weight until 12 or 13 years.

The age changes in the histologic structure of the thymus have been intensively studied by Hammar for the past thirty years. Using the paper weight method,[9] he has determined the weights of the medulla, cortex and connective tissue. Also by a "numerical" method he has estimated the number of the various sizes of Hassall's corpuscles from early fetal life to old age. On page 554 of his review in *Endocrinology,* Hammar [28] gives a detailed description of the age changes in the component parts. The major ones are illustrated in chart 1. The graphs were made from the data in Hammar's summary tables for the normal thymus.[29] From early fetal life until approximately 10 years of age, all the component parts increase in absolute weight; then the medulla and cortex decrease sufficiently to reduce the total thymus weight in spite of an absolute increase in connective tissue and fat. The number of all sizes of Hassall's corpuscles increases from the early fetal period to puberty, and then decreases; the smaller corpuscles are the commonest. Moreover, Hammar's tables also show that the largest sizes, i. e., those over 500 microns in diameter, occur only during the age period of from 6 to 25 years.

In addition, the relative amount of each component part and the number of various sizes of Hassall's corpuscles were calculated for each age period from Hammar's tables. In the fetal period the parenchymatous portions form an increasingly greater proportion of the total weight, while in postnatal life they decrease from 80 per cent of total weight at birth to only 7 per cent in senility (chart 2).

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28. Hammar, J. A.: The New Views as to the Morphology of the Thymus Gland and Their Bearing on the Problem of the Function of the Thymus, Endocrinology **5**:543 and 731, 1921.

29. Hammar, J. A.: Die Lehre vom „Status Thymicus" um Lichte der normalen Thymusverhältnisse, Klin. Wchnschr. **8**:1385, 1929; Ueber die Grundlagen der Lehre des sogenanten Status Thymicolymphaticus, Acta pædiat. **11**:241, 1930. In these articles Hammar reports the summary tables of normal thymuses from his major monograph (footnote 9). The second article is the first and most important of the symposium on "The Physiological and Pathological Significance of the Thymolymphatic System" read at the Second International Pediatrics Congress.

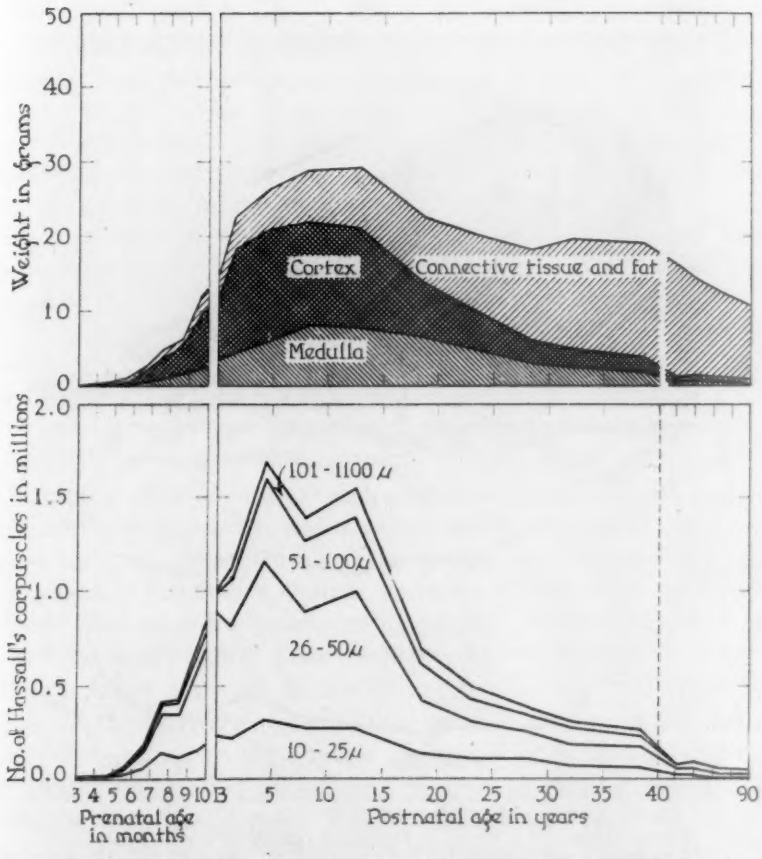

Chart 1.—Graphs of the absolute weight of the component parts of the thymus and of the number of various sized Hassall's corpuscles. The graphs were constructed from the mean values given in Hammar's summary tables (Hammar, J. A.: Ztschr. f. mikr.-anat. Forsch., 1926, supp. vol. 6; 1929, supp. vol. 16; Acta pædiat. **11**:241, 1930). Hammar divided the corpuscles into ten groups according to increasingly sized intervals of diameter, group I consisting of corpuscles from 10 to 25 microns in diameter; group II, from 26 to 50 microns; group III, from 51 to 100 microns; group IV, from 101 to 150 microns; group V, from 150 to 200 microns; group VI, from 201 to 300 microns; group VII, from 301 to 400 microns; group VIII, from 401 to 500 microns; group IX, from 501 to 800 microns, and group X, from 801 to 1,100 microns. The last six groups are combined on the chart. The broken line and the break in shading indicate a change in the age scale.

These figures summarize the major points in the normal growth of the thymus gland with the exception of its variability, which will be discussed later.

Scammon [30] pointed out that the thymus and lymphoid tissue have the same type of growth curve and that no other structure in the

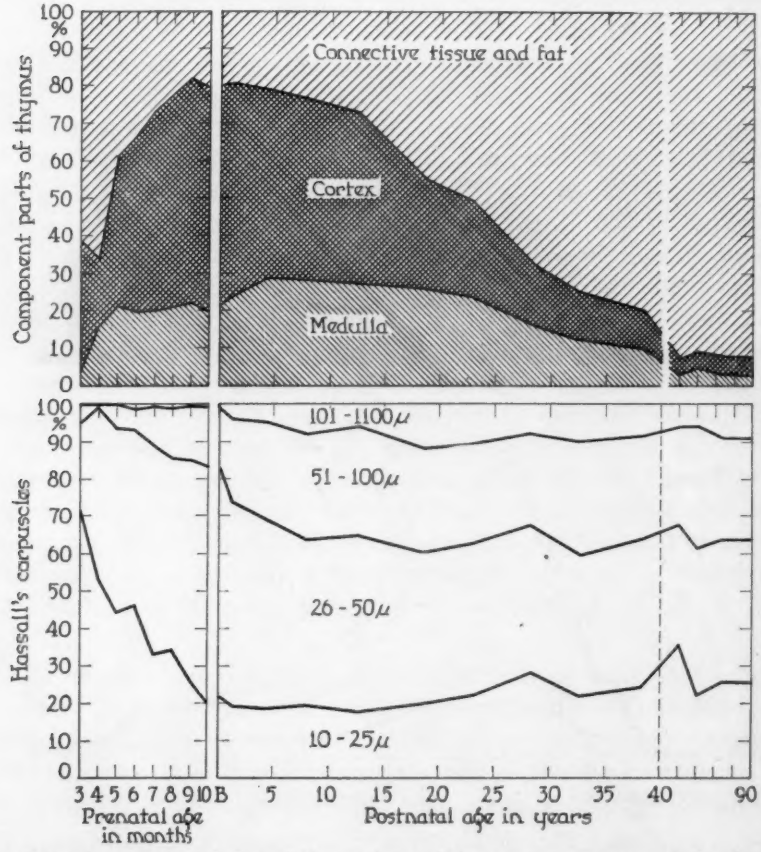

Chart 2.—Graphs of the relative weight of the component parts of the thymus and of the percentage of various sized Hassall's corpuscles. The graphs are based on the data used in chart 1. The broken line and the break in shading indicate a change in the age scale.

body grows in the same manner. Repeatedly, many workers have noted that when the thymus is prominent the lymphoid tissue is also promi-

30. Scammon, R. E.: Developmental Anatomy, in Morris, H.: Morris's Human Anatomy, ed. 8, Philadelphia, P. Blakiston's Son & Co., 1925, p. 5; The Measurement of the Body in Childhood, in Harris, J. A.; Jackson, C. M.; Paterson, D. G., and Scammon, R. E.: The Measurement of Man, Minneapolis, University of Minnesota Press, 1930, p. 173.

nent. Young and Turnbull [15] have recently questioned this association. They found that when age was held constant, the correlation coefficients between the thymus weight and the volume of regional glands were low and frequently insignificant. Hammar,[31] using data from experimental studies on rabbits, obtained essentially the same results.

My personal impression from conducting postmortem examinations on children is that there is a multiplicity of factors that might readily obscure, in mass data, a true association of the size of the thymus and lymphoid tissue. For example, in a case of pneumonia lasting a week or more the thymus and mesenteric lymph nodes are inconspicuous and, as judged by inspection, smaller than those of children killed accidentally, while the pulmonary hilar nodes are red, swollen and conspicuous. Even in children killed accidentally the size of the regional nodes will be influenced by chance local infections, past and present, independent of the general relation of the thymus and lymphoid tissue. Dr. Mead is at present trying to establish normal standards of size for the mesenteric nodes by weighing the ileocecal nodes from children dying of diseases other than those of the gastro-intestinal tract. His work should throw additional light on the subject.

In the current literature,[32] both a broad thymic shadow on an anteroposterior roentgenogram and a narrowing of the trachea on a lateral plate are still considered adequate explanations of most respiratory symptoms. Quantitative absolute measures of the average width of the thymic shadow with measures of its variability for healthy, well nourished and symptom-free children still need to be established. However, using relative measures of the thymic width, Liss,[33] Wasson [22] and Shannon [23] clearly demonstrated that the wide shadows, which are considered diagnostic of the "thymic syndrome" or indications of liability to death from trivial causes, are common in healthy, symptom-free children. On lateral plates, Cooperstock [34] found compression of the trachea by the thymus in 50 per cent of symptom-free infants. Wasson also noted that in spite of high variability, wide shadows tended to occur in overnourished and narrow ones in undernourished infants.

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31. Hammar, J. A.: Zur Frage der Thymusfunktion, Ztschr. f. mikr.-anat. Forsch. **25**:97, 1931.

32. Most of the articles in English will be found in the Archives of Pediatrics, the American Journal of Diseases of Children, the American Journal of Roentgenology and Radiology. A partial review of them is given by Boyd (footnote 5).

33. Liss, I. E.: The Thymic Shadow in Infants, Am. J. Dis. Child. **24**:192 (Sept.) 1922.

34. Cooperstock, M.: Present Concepts of Enlarged Thymus and Status Thymicolymphaticus, J. Michigan M. Soc. **29**:21, 1930.

Incidentally, he has followed the same children for the last decade, and he has not reported any tendency of these children to die of "trivial causes."

These roentgen findings agree with the anatomic ones, that the largest thymuses occur in healthy children killed suddenly by accidents and that the thymus weight-body weight ratio decreases with age. Whether or not the thymus causes respiratory symptoms by pressure [35] is not answered by these findings, but undoubtedly the wide shadows considered evidence of enlargement are instead the normal thymic shadows for well nourished children. Also, these findings invalidate the present common practice of reducing the wide shadow by irradiation, on the principle that it is a sign of a pathologic state in which the child dies unexpectedly of trivial causes, such as ether administered as an anesthetic. Incidentally, I see nothing trivial in an anesthesia, for all the drugs used as such are known to be toxic. Also, absence of a known pathologic condition at autopsy does not signify that the cause of death is trivial, but merely that methods are still inadequate for finding it. For example, a patient with a well established clinical case of diabetes may die in coma or from insulin shock, yet postmortem examination shows nothing to account for death.

During illness and starvation and after irradiation the thymus, like the subcutaneous fat and lymphoid tissue, decreases rapidly in amount. Hammar [36] grouped all these forms of involution under "accidental" in contrast to the age involution already described. According to Friedleben [4] and others,[1] the weight of the thymus in chronic illnesses or malnutrition may be reduced to as little as one-twelfth the normal weight during infancy. For the remainder of childhood Friedleben and I [5] found that disease reduced it to one third of the normal weight.

Hammar and his co-workers [1] found that the thymuses of young rabbits may be reduced to one-half their normal weight in three days of fasting, and to one-fourth in nine days. On refeeding, a distinct increase was found in two days, and normal conditions were established by three weeks. The cortex is reduced more than other parts of the gland, primarily on account of the migration of lymphocytes. Besides the changes in structure due to inanition, Hammar [37] has found

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35. Recent papers questioning the production of most respiratory symptoms by pressure of the thymus are: Wasson, W. W.: Thymic Stridor, J. A. M. A. **89:** 1025 (Sept. 24) 1927. Kennedy, R. L. J., and New, G. B.: Chronic Stridor in Childhood, Sometimes Erroneously Attributed to Enlargement of the Thymus, J. A. M. A. **96:**1286 (April 18) 1931. Pancoast, H. K., and Pendergrass, E. P.: The Modern Roentgenologic Aspect of the Thymus in Infancy, Am. J. Dis. Child. **42:**192 (July) 1931.

36. Hammar (footnotes 10 and 28).

37. Hammar (footnotes 28 and 29).

in certain infections, poisonings and exophthalmic goiter characteristic changes in the cortex-medulla ratio and in the total number and proportion of the various sizes of Hassall's corpuscles. At present, in an attempt to verify his deductions from these changes, he and his co-workers are studying the effect of infections on the thymus of the rabbit. A literal translation of his conclusions [31] is as follows:

> The thymus has no dominance over the lymphoid organs, but according to all appearances both the thymus and lymphoid tissue play a rôle in the resistance-building processes of the organism. These rôles, however, are neither simultaneous nor identical. The reaction of the thymus starts very early and is expressed in the formation of Hassall's corpuscles. The reaction of the lymphoid tissue appears definitely later and results in a formation of secondary follicles apparently proceeding parallel with the formation of antibodies.

No other work comparable with that of Hammar and his students has been done on the structural changes in disease.

Since most subjects who come to autopsy have been ill for more than three days, the pathologist's eye becomes adjusted to the involuted thymuses, so that the prominent thymus of the healthy, well nourished subject appears enlarged to him. In other words, the anatomic picture called status thymicolymphaticus is the normal state of the thymus and lymphoid tissue of the healthy person. The inconspicuous thymus and lymphoid tissue, commonly called normal, is the involuted thymus and lymphoid tissue of the poorly nourished or diseased person.

The objection is still made that even if not enlarged the thymus may have a disturbed endocrine function. Theoretically this objection is valid, but factually Park and McClure [38] were unable to demonstrate any effects following the complete extirpation of the thymus on the growth of puppies. In reviewing the literature, they found that the symptoms and signs considered to be due to removal of the gland could be, in the main, accounted for by environmental conditions. In short, the existence of a thymic hormone in mammals has never been adequately demonstrated. The true hypertrophy of the thymus in exophthalmic goiter has been considered evidence of a multiglandular function, but Hammar considered it the response of the thymus to a toxic substance. Likewise, Scammon [39] found no significant correlation between the weights of the thymus and those of the thyroid in healthy young men killed in battle.

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38. Park, E. A., and McClure, R. D.: The Results of Thymus Extirpation in the Dog, Am. J. Dis. Child. **18**:317 (Nov.) 1919.

39. Scammon, R. E.: A Note on the Relation Between the Weight of the Thyroid and the Weight of the Thymus in Man, Anat. Rec. **21**:25, 1921.

GRAPHIC ANALYSIS

The foregoing review indicates that because of "accidental" involution only thymuses from persons dying shortly after the onset of illness can be used in establishing a standard of normal weight. Since the concept status thymicolymphaticus still persists, the thymuses must be limited to those from persons killed by accidents. Since most fatal illnesses cause more or less inanition, allowance should be made for the effect of inanition on the weight of the thymus before estimating the specific effect of a given disease on the thymus. Rough estimates of the general inanition of the body can be obtained from two usually reported items, the duration of the illness and the pathologist's description of the nutritional state. In a previous report,[5] when the data were divided according to two major nutritional ranks, well nourished and poorly nourished, a comparison of nutritional ranks and height-weight indexes demonstrated that the estimations of nutrition were highly unreliable. On the other hand, the time of injury or the appearance of symptoms is reported with reasonable accuracy. Although symptoms occur late in some diseases, the duration of symptoms is probably a good approximation of the length of time the disease has caused general inanition.

In order to measure this effect of inanition, as well as of age and disease, on the size of the thymus, only individual case reports could be used which gave the duration of the illness as well as the age, the weight of the thymus and the diagnosis. Of the approximately 10,000 autopsies performed from 1910 to 1929 by the department of pathology of the University of Minnesota, because the thymus is not weighed as a routine measure, only 1,065 records contained the necessary data. Of these, 234 were for stillborn fetuses measuring 45 cm. or more in total body length. The remaining 831 records are insufficient for an analysis including all ages, and therefore the literature was searched for additional case reports containing the necessary information. For the postnatal period, 1,060 such case reports were found, 92 from Friedleben,[4] 26 from von Mettenheimer,[40] 36 from Dustin and Zunz [41] and 906 from Hammar.[9] Friedleben's data were primarily for young children, von Mettenheimer's for children dying of infectious diseases, Dustin and Zunz' for young adult men killed in war and Hammar's for all ages and all diseases.

These combined data, consisting of 1,891 case records for postnatal life, were first divided into five year age periods; then, since the data for

40. von Mettenheimer, H.: Zum Verhalten der Thymusdrüse im Gesundheit und Krankheit, Jahrb. f. Kinderh. **46**:55, 1898.

41. Dustin, A. P., and Zunz, E.: A propos des corrélations fonctionnelles entre le thymus et le corps thyroïde, J. de physiol. et de path. gén. **17**:905, 1918.

late adult life were scanty, two or more such periods were combined, and, since growth in infancy is rapid, the first period was subdivided. The cases were arranged in three categories for the duration of illness within each age group: (*A*) ill less than twenty-four hours; (*B*) ill from one to seven days, and (*C*) ill one week or more. Within these time periods for each age the cases were finally divided according to six diagnostic categories, namely: (*a*) accidents, including trauma, poisoning, electrocution and drowning; (*b*) undetermined causes, including "status thymicolymphaticus" and cases in which pathologic or clinical findings were considered inadequate to account for death; (*c*) infections; (*d*) congenital defects, except monstrosities, which were omitted entirely; (*e*) miscellaneous causes, consisting of all cases not in the preceding or following categories, and (*f*) exophthalmic goiter and leukemia.

All the unpublished data from the department of pathology of the University of Minnesota, the published data of Friedleben,[4] as his monograph is not readily available today, and the case numbers of the other authors are given in table 1, arranged according to the categories just defined.

Considerable difficulty was experienced in classifying subjects with more than one diagnosis. In general, they were placed under the condition with which the fatal illness seemed to begin. No attempt was made to follow the "International List of Causes of Death" used in vital statistics. For instance, intestinal obstruction from adhesions due to peritonitis was classified as an "infection" if the patient had had a continuous illness, but as a "miscellaneous cause" if there had been an interim of good health between the acute peritonitis and the intestinal obstruction. Also, all congenital defects were classified together, although death was usually caused by an intercurrent disease. Since many defects do not seriously affect the general health of the subject, illness was considered as starting with the onset of symptoms.

According to Hammar's criteria, the group "accidents, ill less than twenty-four hours" may be considered a sample of normal persons, and the weights of their thymuses may be used to establish a standard of the size and variability of the normal thymus. After trying various statistical methods, a standard was obtained by calculating for each age group the median weight or 50 percentile, the 25 and 75 percentiles, the interquartile range in weight (i. e., the range from 25 to 75 percentile), the 10 and 90 percentiles and the range in weight from 10 to 90 percentile [42] (table 2). By definition of these terms, 50 per cent

42. The graphic method used in obtaining these percentiles is described by Yule, G. U.: An Introduction to the Theory of Statistics, ed. 6, London, C. Griffin & Company, 1922, p. 150.

TABLE 1.—*Thymus Weights Arranged According to Age, Duration of Illness and Cause of Death*

Source and Number	Age	Sex	Height of Body, Cm.	Weight of Body, Gm.	Nutritional Rank	Duration of Illness	Weight of Thymus, Gm.	Cause of Death*
1. Birth to 24 Hours—A. Ill Less Than Twenty-Four Hours—a. Accidents								
A-25— 142	Few mins.†	M	52.0	3,400	+++	?	25.0	Suffocation; homicide
A-28—1472	Few mins.†	M	50.0	2,886	+++	?	11.0	Homicide
A-27— 337	3 mins.	M	53.0	3,110	+++	Life	7.8	Birth trauma
A-15— 145	5 mins.†	F	47.0	.....	+++	Life	8.9	Birth trauma
A-25— 922	10 mins.	F	47.5	2,260	+	Life	9.0	Birth trauma
A-27—1231	10 mins.	F	50.0	3,000	+++	Life	9.0	Birth trauma
A-26— 530	15 mins.	M	53.0	3,210	+++	Life	12.0	Birth trauma
A-25— 642	34 mins.	M	56.0	4,150	+++	Life	18.0	Birth trauma
A-20— 35	½ hr.	F	49.0	.....	++++	Life	13.0	Birth trauma
A-23— 587	½ hr.	F	55.5	3,260	+++	Life	12.0	Birth trauma
A-27— 721	½ hr.	M	55.5	4,660	+++	Life	12.0	Birth trauma
A-21— 67	Few hrs.†	F	54.5	3,500	+++	?	18.0	Strangulation; homicide
A-25— 425	Few hrs.†	M	50.0	2,830	+++	Life	15.0	Hemorrhage from untied cord
A-25— 194	Few hrs.†	M	55.0	3,770	+++	Life	16.0	Birth trauma
A-25— 344	Few hrs.†	F	52.0	3,145	+++	Life	15.0	Birth trauma
A-24— 742	1¼ hr.	M	55.0	3,200	+++	Life	11.0	Birth trauma
A-24— 476	2 hrs.	M	54.0	.....	++++	Life	12.0	Birth trauma
A-16— 172	2 hrs.	M	46.0	.....	+++	Life	9.5	Birth trauma
A-28— 646	2 hrs.	M	48.0	2,750	+++	Life	11.0	Birth trauma
A-24— 720	3 hrs.	F	50.0	3,200	+++	Life	19.5	Birth trauma
A-27— 681	3 hrs.	M	48.0	.....	+++	Life	10.0	Birth trauma
A-28—1666	3 hrs.	M	48.0	.....	+++	Life	12.1	Birth trauma
A-21— 7	3½ hrs.	M	53.0	3,275	+++	Life	31.0	Birth trauma
A-27— 46	3½ hrs.	M	46.0	2,070	+++	Life	9.6	Birth trauma
A-25— 275	4 hrs.	M	48.5	2,400	+++	Life	7.8	Birth trauma
A-24— 295	5 hrs.	M	49.0	2,605	++	Life	17.5	Birth trauma
A-27— 713	5 hrs.	M	46.0	2,373	++	Life	6.0	Birth trauma
A-28—1637	5 hrs.	M	47.0	2,381	+	Life	13.0	Birth trauma
A-24— 350	5 hrs.	F	45.0	.....	+++	Life	10.0	Birth trauma
A-28— 84	5 hrs.	M	52.0	3,160	+++	Life	30.0	Birth trauma
A-24— 58	5 hrs.	F	50.0	.....	+++	Life	14.3	Birth trauma
A-26— 453	5½ hrs.	F	52.0	3,150	+++	Life	8.7	Birth trauma
A-25— 788	5½ hrs.	M	56.0	3,920	+++	Life	19.5	Birth trauma
A-28— 913	6 hrs.	F	45.0	1,650	++	Life	9.8	Birth trauma
A-27— 157	6½ hrs.	F	50.0	3,200	+++	Life	12.0	Birth trauma
A-23— 535	8 hrs.	F	60.0	6,750	++++	Life	10.0	Birth trauma
A-29—1204	8 hrs.	M	56.0	3,175	+++	Life	15.0	Birth trauma
A-28—1555	9 hrs.	M	46.0	1,815	++	Life	11.5	Birth trauma
A-25— 453	9 hrs.	F	51.0	3,200	+++	Life	17.0	Birth trauma
A-26— 356	9 hrs.	M	45.0	2,015	+++	Life	9.0	Birth trauma
A-25— 775	10 hrs.	M	48.0	2,890	+++	Life	17.1	Birth trauma
A-15— 331	11 hrs.	M	55.0	.....	+++	Life	7.6	Birth trauma
A-27— 922	11 hrs.	F	46.5	.....	++++	Life	16.4	Birth trauma
A-26— 449	11½ hrs.	M	48.0	2,480	+++	Life	8.0	Birth trauma
A-25— 989	12 hrs.	F	49.0	2,350	++	Life	3.5	Birth trauma
A-29—1430	12 hrs.	M	53.0	.....	+++	Life	13.0	Birth trauma
A-26— 766	12½ hrs.	M	47.0	2,150	+++	Life	11.0	Birth trauma
	12½ hrs.	F	53.0	3,380	+++	Life	9.0	Birth trauma

A-26— 706	12½ hrs.	M	47.0	2,150	+++	Life	11.0	Birth trauma
A-27— 86	12½ hrs.	F	53.0	3,380	+++	Life	9.0	Birth trauma
A-27— 179	14¾ hrs.	M	52.0	.....	+++	Life	6.5	Birth trauma
A-24— 84	18 hrs.	M	56.0	3,600	+++	Life	8.0	Hemorrhage from cord
A-29—1467	18 hrs.	F	47.0	3,175	+++	Life	10.0	Birth trauma
A-25— 908	20 hrs.	F	46.5	.....	+++	Life	8.0	Birth trauma
A-25— 920	20 hrs.	M	54.0	.....	+++	Life	9.0	Birth trauma
A-29— 514	23 hrs.	M	48.0	2,345	+	Life	15.0	Birth trauma
A-27— 548	23 hrs.	F	45.5	2,100	+++	Life	6.8	Birth trauma
Hammar, no. 1743								
				b. Undetermined Causes				
A-20— 339	Few mins.†	M	56.0	3,460	+++	?	10.0	Strangulation ?
A-24— 171	Few mins.†	F	51.6	3,200	++++	?	14.0	Mother unattended
A-27—1100	Few mins.†	F	50.0	2,985	++	?	5.0	Cord untied
A-16— 274	Few mins.†	M	47.0	.....	+++	?	17.0	Suffocation ?
A-28—1009	Few mins.†	F	45.5	1,900	+++	?	13.5	
A-22— 30	10 mins.	M	55.5	3,530	++++	Life	13.0	Cord around neck
A-22— 154	Few hrs.†	F	54.0	3,780	+++	?	15.0	Strangulation ?
A-25— 102	Few hrs.†	M	52.0	4,300	++++	?	12.0	Neglected
A-21— 139	Few hrs.†	F	51.5	3,475	+++	?	12.0	Homicide ?
A-24— 12	½ hr.	F	53.0	3,220	+++	Life	13.2	Placenta previa
A-28— 362	1 hr.	M	48.5	2,975	+++	Life	7.7	
A-23— 530	2½ hrs.	M	56.0	.....	++++	Life	35.0	Thyroid 18 Gm.
A-24— 104	3 hrs.	F	51.0	3,100	+++	Life	10.0	
A-22— 269	4 hrs.	F	51.0	3,320	+++	Life	10.0	
A-21— 573	4 hrs.	M	47.5	.....	++	Life	10.0	Birth trauma ?
A-27— 28	4 hrs.	F	45.0	2,100	++	Life	14.0	
A-18— 252	4½ hrs.	F	51.0	3,270	+++	Life	17.0	Birth trauma ?
A-17— 220	4½ hrs.	F	....	2,975	+++	Life	12.0	Birth trauma ?
A-25— 317	5 hrs.	M	45.0	1,720	+++	Life	3.2	
A-23— 750	6 hrs.	F	45.0	2,060	+++	Life	7.0	In labor 51 hours; cesarean section
A-24— 642	6 hrs.	M	47.5	1,880	++	Life	9.0	
A-26— 778	7 hrs.	M	47.4	2,140	++	Life	7.0	
A-27— 916	7 hrs.	M	46.0	2,110	++	Life	15.0	
A-28—1092	7 hrs.	M	45.0	2,300	+++	Life	13.0	
A-25— 39	8 hrs.	M	45.0	1,810	+++	Life	8.5	
A-25— 687	8 hrs.	F	48.0	2,800	+++	Life	4.0	
A-25— 428	9 hrs.	M	47.0	1,953	+++	Life	12.9	
A-24— 116	9 hrs.	F	51.0	2,145	++	Life	6.0	Face presentation
A-23— 300	12 hrs.	M	54.5	3,650	+++	Life	12.0	
A-29—1506	12 hrs.	F	47.0	.....	+++	Life	12.0	
A-23— 41	13 hrs.	F	46.0	2,241	+++	Life	7.5	
A-25— 659	13 hrs.	F	47.0	.....	+++	Life	8.5	Hemorrhagic condition of lungs
A-26— 975	13 hrs.	F	46.0	2,325	++++	Life	7.5	
A-24— 454	14 hrs.	F	46.0	1,540	+	Life	3.0	
A-28— 916	15 hrs.	M	46.5	1,900	++	Life	5.0	
A-28—1596	15 hrs.	M	47.0	2,600	++	Life	8.0	
A-28— 885	18 hrs.	M	50.0	.....	+++	Life	12.0	Birth trauma ?
A-23— 193	19 hrs.	F	50.0	3,560	+++	Life	9.0	
A-26— 776	19 hrs.	F	51.5	3,100	+++	Life	11.0	Stridor; thyroid 11 Gm.
A-28—1241	21 hrs.	M	49.0	2,790	+++	Life	10.0	
A-16— 248	24 hrs.	M	48.0	.....	+++	Life	7.3	Birth trauma ?
Hammar, nos. 994 and 1728								

* Besides the cause of death, any incidental finding that might give a clue to the cause of death is listed in this column. Also, if in the opinion of the pathologist the child probably died of a given cause but the evidence was inconclusive, this cause is followed by a question mark.

† Approximate.

TABLE 1.—*Thymus Weights Arranged According to Age, Duration of Illness and Cause of Death—Continued*

Source and Number	Age	Sex	Height of Body, Cm.	Weight of Body, Gm.	Nutritional Rank	Duration of Illness	Weight of Thymus, Gm.	Cause of Death
1. Birth to 24 Hours—A. Ill Less Than 24 Hours—Continued—c. Infections								
A-23— 367	1 hr.	F	49.0	2,135	++	Life	11.0	Congenital syphilis
A-28— 920	1 hr.	M	45.0	2,130	++	Life	5.7	Congenital syphilis
A-24— 722	6½ hrs.	M	45.0	2,480	++	Life	3.5	Congenital syphilis
A-15— 314	8 hrs.	M	49.0	.....	+++	Life	3.5	Congenital syphilis
A-24— 63	12 hrs.	F	45.0	2,310	+++	Life	5.0	Congenital syphilis
A-18— 157	12 hrs.	M	52.5	.....	+++	Life	8.0	Congenital syphilis
Hammar, nos. 993, 1347 and 1722								
d. Congenital Defects								
A-28— 788	Few mins.†	F	47.5	2,940	+++	Life	4.3	Hypertrophied kidneys; birth trauma
A-25— 604	2 min.	F	49.0	2,800	+++	Life	10.5	Spina bifida; birth trauma
A-25— 8	1 hr.	F	52.0	3,400	+++	Life	11.0	Hydrocephalus; birth trauma
A-26—1159	1 hr.	M	57.0	.....	+++	Life	8.5	Multiple defects
A-28— 476	1½ hrs.	M	47.0	.....	++	Life	12.5	Multiple defects
A-25— 527	3 hrs.	M	53.0	3,280	+++	Life	12.0	Diaphragmatic hernia; birth trauma
A-24— 312	5 hrs.	M	54.0	4,140	+++	Life	16.9	Diaphragmatic hernia
A-28— 816	10½ hrs.	F	51.5	.....	+++	Life	13.0	Bilateral cleft palate
A-24— 662	12 hrs.	F	52.0	.....	+++	Life	6.0	Congenital inspiratory stridor
A-20— 142	12 hrs.	M	47.0	2,080	++	Life	5.0	Cystic kidneys
A-28—1516	14 hrs.	F	53.0	2,150	+	Life	15.0	Meningocele
A-27— 395	18 hrs.	M	50.5	3,760	+++	Life	22.1	Meningo-encephalocele
A-24— 36	20 hrs.	M	56.0	5,000	+++	Life	15.0	Enlarged heart
Hammar, no. 1444								
e. Miscellaneous Causes								
A-26— 566	½ hr.	F	52.0	.....	+++	Life	6.0	Hemolytic jaundice
A-22— 310	3 hrs.	F	51.0	3,600	+++	Life	12.0	Hemorrhagic disease
A-22— 16	16 hrs.	F	48.0	2,340	+++	Life	6.0	Hemorrhagic disease
Hammar, no. 1533								
2. 1 Day to 1 Year—A. Ill Less Than Twenty-Four Hours—a. Accidents								
A-23— 598	44 hrs.	M	51.0	2,940	++	20 hrs.	7.9	Birth trauma
A-24— 394	9 days	M	55.0	4,000	+++	Few hrs.†	12.0	Birth trauma
A-23— 515	3 wks.	M	53.0	2,890	+++	4 hrs.	11.0	Poisoning with compound solution of cresol
A-25— 256	7 wks.	M	56.5	.....	+++	Found dead	20.0	Aspiration of foreign substance
A-27— 777	7 wks.	F	61.5	.....	+++	1 day	30.0	Cerebral hemorrhage
A-24— 809	3 mos.	F	58.0	.....	+++	Found dead	25.0	Carbon monoxide poisoning
A-28— 733	4 mos.	M	63.0	.....	+++	Found dead	29.0	Carbon monoxide poisoning
Hammar, nos. 813, 1767, 1480 and 910								
b. Undetermined Causes								
A-26— 4	1¼ days	F	52.0	3,120	++	6 hrs.	16.5	
A-26— 990	2 days	M	52.0	3,500	++++	Few hrs.†	6.0	Birth trauma ?
A-22— 264	2 days	M	50.0	3,300	+++	Sudden death	8.0	
A-25— 291	2½ days	F	54.0	3,625	+++	Found dead	9.3	Tracheobronchitis; "cold"
A-25— 867	3½ days	M	50.0	2,860	+++	Sudden death	7.0	
A-22— 592	4 days	M	50.0	3,360	+++	Found dead	12.0	
A-28— 18	7 days	F	52.0	3,375	+++	Life	4.0	Pneumonia ?; birth trauma ?
	11 days	M	56.0	.....	+++	Found dead	15.0	
						Found dead	3.5	

A-28— 18	7 days	F	52.0	3,375	+++	Life	4.0	Pneumonia ?; birth trauma ?
A-17— 20	11 days	M	56.0	.....	+++	Found dead	15.0	
A-23— 608	13 days	F	52.5	2,980	++	Found dead	3.5	
A-20— 258	15 days	M	51.5	3,005	+++	Few mins.†	12.5	Suffocation ?
A-28—1253	18 days	F	52.0	3,250	++	1 day	11.0	Temperature 106 F.
A- 9— 958	3 wks.	M	56.0	.....	+++	Sudden death	22.0	Pneumonia ?
Friedleben 236	25 days	..	....	1,936	+	Sudden death	4.0	Congestion of intestinal mucosa; edema of brain
A-23— 359	26 days	M	48.0	3,000	+++	Few mins.†	15.4	
Friedleben 237	4 wks.	..	....	.....	+++	Sudden death	14.8	Hyperemia of lungs
A-19— 234	6 wks.	M	....	3,840	+++	Found dead	28.0	Asphyxia ?
A-19— 241	6 wks.	F	54.0	.....	+++	Found dead	30.0	
A-23— 301	6 wks.	M	61.0	.....	+++	Found dead	40.0	Edema of lungs
A-25— 337	6 wks.	F	56.0	4,040	+++	Found dead	20.0	Pneumonia ?
A-23— 652	7 wks.	F	58.0	5,850	+++	Found dead	25.0	
Friedleben 240	2 mos.	M	....	.....	+++	Found dead	31.8	Cerebral edema
A-10— 125	2 mos.	F	57.0	.....	+++	12 hrs.	13.0	
A-19— 223	2 mos.	M	61.0	5,132	+++	Found dead	22.0	
Friedleben 244	2½ mos.	M	....	.....	+++	12 hrs.	18.6	Cerebral edema
A-22— 440	3 mos.	M	62.0	.....	+++	Found dead	40.0	
A-26— 508	3 mos.	M	60.0	4,900	+++	2 hrs.	30.0	
A-23— 684	3½ mos.	M	70.0	.....	++++	Found dead	38.0	Old tentorial tear; generalized spasticity
A-22— 500	4 mos.	M	....	.....	++++	Sudden death	28.6	
A-24— 658	4 mos.	F	66.3	.....	++++	Found dead	17.5	
A-24— 825	4 mos.	M	63.0	5,180	+++	Sudden death	25.0	Slight "cold"; convulsion
A-21— 47	4 mos.	F	56.0	4,530	++	12 hrs.	10.0	
A-19— 294	4 mos.	..	....	.....	+++	11 hrs.	30.0	Septicemia ?
A-28— 473	4 mos.	F	....	.....	+++	8 hrs.	23.0	Pulmonary edema; respiratory rate 100
A-28— 510	4 mos.	F	63.0	.....	+++	12 hrs.	18.3	Bacteria in lungs
A-17— 103	5 mos.	F	59.0	.....	++++	Sudden death	13.5	
A-26— 698	5 mos.	F	63.0	.....	+++	Found dead	20.7	
A-26—1042	5 mos.	M	67.0	6,910	++++	Sudden death	65.0	
A-23— 479	5 mos.	F	60.0	.....	++	Sudden death	4.0	Eczema; acute ileocolitis; feeding case
A-28—1328	5 mos.	F	....	3,275	++	Sudden death	5.0	Edema of lungs
Friedleben 255	5 mos.	M	....	3,431	++	Sudden death	14.5	Mors thymica
A-24— 140	6 mos.	F	70.0	9,000	++++	Found dead	34.0	
A-28— 578	6 mos.	M	68.0	.....	+++	Found dead	46.5	Pulmonary edema; pillow over face
A-22— 216	7 mos.	M	62.0	.....	+++	Sudden death	15.0	Feeding case until 2 weeks before death
A- 9— 942	7 mos.	F	67.0	.....	+++	5 hrs.	35.0	Congestion of brain
A-18— 205	7½ mos.	M	73.0	.....	+++	23 hrs.	49.0	"Cold"; temperature, 104 F.
Friedleben 274	8 mos.	M	....	5,378	++	Sudden death	12.9	
Friedleben 273	8 mos.	M	....	6,197	+++	Sudden death	17.3	Diarrhea and wasting
A-26—1132	8 mos.	M	67.5	.....	+++	Few mins.	38.1	Streptococcus in lungs
Friedleben 277	9½ mos.	F	....	9,324	+++	Sudden death	33.2	Fatty degeneration of liver
A-24— 232	10 mos.	F	....	.....	++++	Found dead	17.6	
A-26—1071	10 mos.	M	72.0	.....	+++	Sudden death	18.0	Heart 82 Gm.
Hammar, nos. 948, 810, 1152, 812, 1000, 946, 947, 1529, 1544, 1506, 1507, 1524, 1618, 444, 781, 808, 809, 953, 1530, 955, 944, 780, 952, 787, 964, 970, 1838, 1406, 1509, 1416, 1841, 811, 1489, 976, 779, 1576, 1531 and 949								

c. Infections

A-26— 964	2 days	M	52.0	3,775	+++	Found dead	12.0	Aspiration pneumonia
A-27— 288	3 days	F	52.5	.....	+++	8 hrs.	7.6	Aspiration pneumonia

TABLE 1.—*Thymus Weights Arranged According to Age, Duration of Illness and Cause of Death—Continued*

Source and Number	Age	Sex	Height of Body, Cm.	Weight of Body, Gm.	Nutritional Rank	Duration of Illness	Weight of Thymus, Gm.	Cause of Death
2. 1 Day to 1 Year——A. Ill Less Than Twenty-Four Hours——c. Infections—Continued								
A-23— 758	11 days	M	52.0	2,850	++	Few hrs.	10.0	Pneumonia
A-25— 69	3 wks.	M	54.0	.....	++++	Sudden death	10.0	Abscess of lung; pneumonia
A-26— 946	4 wks.	F	53.0	.....	+++	Sudden death	5.9	Pneumonia
A-25— 899	1 mo.	M	52.0	.....	++	Found dead	15.0	Pneumonia
A-27— 634	2 mos.	M	58.0	5,400	++++	1 day	30.2	Pneumonia
A-26— 582	2 mos.	M	55.0	3,790	++	Found dead	17.0	Pneumonia
A-29—1025	2½ mos.	M	82.0	5,200	+++	Found dead	30.0	Pneumonia
A-22— 598	3 mos.	M	62.0	.....	++	14 hrs.	21.0	Acute splenitis; bronchitis
A-29—1646	3 mos.	M	62.5	5,595	+++	Found dead	25.0	Pneumonia
A-29— 169	4 mos.	M	83.0	.....	++	Found dead	20.0	"Cold"; pneumonia
A-26— 937	4 mos.	M	62.0	.....	++++	Found dead	45.0	Pneumonia
A-28—1425	4 mos.	M	64.0	.....	+++	Found dead	40.0	Pneumonia
A-29—1397	6 mos.	F	55.0	.....	++	Found dead	20.0	Pneumonia
A-29—1609	7 mos.	M	....	6,300	+++	18 hrs.†	15.0	Pneumonia; mastoiditis
A-26—1133	8 mos.	M	72.0	.....	++++	12 hrs.	17.0	Pneumonia
A-27— 694	8 mos.	F	69.0	.....	+++	16 hrs.	11.0	Pneumonia
A-24— 810	9 mos.	M	71.0	.....	++++	Found dead	42.0	Pneumonia
Hammar, nos. 1435, 929, 975, 1041, 1827, 951, 966, 1343, 1042 and 954								
d. Congenital Defects								
A-28— 866	2 days	M	47.0	2,400	++	Found dead	3.7	Cardiac defect
A-28— 635	4½ days	F	50.5	2,730	++	1½ hrs.	3.5	Cardiac defect; birth trauma
A-26— 693	6 mos.	F	58.0	4,460	+++	Sudden death	13.4	Clubfoot; postoperative pneumonia; microcephaly
A-25— 110	9 mos.	M	66.0	.....	++	6 hrs.	4.0	Cardiac defects; pneumonia
e. Miscellaneous Causes								
A-28— 700	36 hrs.	F	52.5	.....	+++	6 hrs.†	7.0	Gangrene of intestine
A-24— 300	2 days	F	51.0	2,800	+++	4 hrs.	16.0	Hemorrhage from duodenal ulcer
A-26— 304	2 days	M	50.5	.....	+++	30 mins.	9.1	Splenomegaly
A-15— 255	3 days	F	48.0	.....	+++	10 hrs.†	7.5	Hemorrhage from duodenal ulcer
A-26— 888	4 days	M	51.5	3.500	+++	7 hrs.†	20.0	Splenomegaly
Friedleben 251	3½ mos.	M	....	6.548	+++	Sudden death	24.4	Sudden laryngismus
A-27— 6	4½ mos.	M	59.0	4,980	++	Found dead	10.0	Cardiac enlargement; pneumonia
Friedleben 278	10 mos.	M	....	7,176	+++	Sudden death	26.8	Laryngismus; intestinal catarrah
Hammar, nos. 1470, 1469 and 1587								
B. Ill from One to Seven Days——a. Accidents								
A-18— 79	1 day	F	53.0	.....	+++	Life	11.8	Birth trauma
A-25—1053	1 day	F	46.0	3,000	++	Life	10.5	Birth trauma
A-28—1551	1 day	M	55.5	3,910	+++	Life	15.0	Birth trauma
A-29—1595	1 day	M	45.0	3,175	+++	Life	14.5	Birth trauma
A-25— 273	28 hrs.	M	50.0	2,580	+++	Life	8.0	Birth trauma
A-26— 836	29 hrs.	M	52.0	.....	+++	Life	22.0	Birth trauma
A-25— 77	32 hrs.	M	48.0	2,410	+++	Life	7.4	Birth trauma
A-28—1430	32 hrs.	M	52.0	3,400	+++	Life	15.0	Birth trauma
A-23— 221	34 hrs.	M	54.0	4,530	+++	Life	18.0	Birth trauma
A-23— 778	36 hrs.	M	55.0	3,400	+++	1 day	9.0	Birth trauma
A-24— 414	36 hrs.	M	48.0	.....	+++	Life	8.0	Birth trauma
					++	Life	10.0	Birth trauma

A-23— 778	36 hrs.	M	55.0	3,400	+++	1 day	9.0	Birth trauma
A-24— 414	36 hrs.	M	48.0	.....	+++	Life	8.0	Birth trauma
A-24— 727	1½ days	M	50.0	.....	++	Life	10.0	Birth trauma
A-15— 346	40 hrs.	M	48.5	.....	+++	Life	6.4	Birth trauma; mother received scopolamine and morphine
A-29—1287	40 hrs.	F	50.0	3,630	+++	Life	12.0	Birth trauma
A-16— 140	2 days	M	51.5	.....	+++	Life	4.5	Birth trauma
A-28— 77	2 days	M	47.5	2,020	++	Life	3.1	Birth trauma
A-26— 800	2 days	M	54.0	.....	+++	Life	7.0	Birth trauma
A-28— 354	2 days	M	51.0	2,850	+++	Life	5.3	Birth trauma
A-28— 502	2 days	M	53.0	.....	+++	Life	5.4	Birth trauma
A-29— 830	2 days	M	50.0	3,010	+++	1 day	18.0	Birth trauma
A-28—1462	2 days	M	57.0	3,875	+++	1 day	20.0	Birth trauma
A-21— 509	2½ days	M	50.0	2,945	++	Life	7.5	Birth trauma
A-27—1265	3 days	M	47.0	2,045	++	1 day†	6.0	Birth trauma
A-24— 328	3 days	M	56.5	4,225	+++	1 day†	11.9	Birth trauma; temperature, 104 F.
A-26— 884	3 days	F	51.5	.....	+++	Life	8.0	Birth trauma
A-27—1163	3 days	M	46.0	1,910	+++	Life	4.9	Birth trauma
A-25— 139	3 days	M	50.5	2,660	++	1 day	5.5	Birth trauma; hemorrhagic disease
A-27— 602	3 days	F	51.4	2,950	++	Life	5.4	Birth trauma
A-23— 403	4 days	M	56.9	3,415	+++	1 day	12.0	Rupture of liver
A-23— 264	10 days	F	49.0	3,600	+++	3 days	8.0	Birth trauma
A-26—1020	4 days	M	49.0	2,100	++	Life	3.6	Birth trauma
A-26— 735	4 days	F	57.0	4,200	+++	Life	13.0	Birth trauma
A-26— 933	4 days	F	49.0	.....	+++	Life	5.0	Birth trauma
A-27— 402	4 days	M	54.0	.....	+++	Life	5.0	Birth trauma
A-30— 123	5 days	M	55.0	.....	+++	Life	6.5	Birth trauma
A-18— 75	6 days	M	47.0	.....	+++	Life	7.2	Birth trauma
A-21— 202	6 days	M	....	3,000	+++	Life	5.0	Birth trauma
A-27— 809	2½ mos.	M	56.5	.....	+++	5 days	6.0	Second degree burns from steam kettle; pneumonia
A-23— 612	9 mos.	M	72.0	.....	+++	1 day	15.0	Peanut in trachea
Hammar, nos. 1473, 786, 430, 1711, 1516, 1632, 1008 and 985								

b. Undetermined Causes

A-23— 752	1 day	M	47.0	2,500	+++	Life	5.6	
A-24— 416	1 day	M	47.5	2,100	+	Life	6.0	
A-24— 503	1 day	M	46.0	.....	++	Life	5.0	
A-26—1031	1 day	F	47.0	.....	+	Life	2.3	
A-28— 870	1 day	M	48.0	2,755	+++	Life	4.3	
A-23— 625	28 hrs.	F	50.5	.....	+++	Life	5.0	
A-26— 40	29 hrs.	M	45.0	2,100	++	Life	10.0	
A-24— 485	30 hrs.	F	47.0	.....	++	Life	5.0	
A-23— 350	36 hrs.	F	54.0	.....	+++	Life	15.0	
A-22— 24	36 hrs.	F	45.5	1,170	++	Life	10.0	
A-15— 232	41 hrs.	M	....	.....	++	Life	3.8	
A-24— 222	2 days	M	51.3	3,510	+++	Life	8.5	Face presentation
A-28— 656	2 days	M	51.0	.....	+++	1 day	7.0	
A-27— 613	3 days	M	48.0	2,430	++	Life	9.1	
A-22— 22	4 days	F	45.0	2,300	+++	1 day	4.0	
A-23— 210	4 days	F	50.0	.....	+++	2 days	8.0	
A-24— 127	4 days	M	48.0	2,280	+	3 days	8.2	
A-22— 244	4 days	M	45.5	.....	++	Life	10.0	
A-24— 601	4 days	M	47.0	.....	+++	Life	8.0	
A-22— 470	5 days	F	54.0	3,400	+++	1 day	8.0	
A-23— 22	5 days	M	45.0	.....	++	Life	10.0	

TABLE 1.—*Thymus Weights Arranged According to Age, Duration of Illness and Cause of Death—Continued*

Source and Number	Age	Sex	Height of Body, Cm.	Weight of Body, Gm.	Nutritional Rank	Duration of Illness	Weight of Thymus, Gm.	Cause of Death
2. 1 Day to 1 Year—B. Ill from One to Seven Days—b. Undetermined Causes—Continued								
A-23— 151	5 days	M	50.0	.....	++	Life	4.0	Edema of subcutaneous tissues
A-24— 455	11 days	M	47.0	2,130	++	5 days	3.0	
A-22— 95	14 days	M	45.0	2,875	+	2 days	9.0	Diarrhea
A-26— 374	20 days	F	53.0	2,265	+	6 days	2.0	Fatty degeneration of liver
A-25— 943	1 mo.	M	50.0	2,860	+	4 days	4.5	
A-24— 794	31 days	M	50.0	2,410	+	3 days	6.0	
A-25— 107	5 wks.	M	50.0	2,800	++	2 days	8.0	Pneumonia ?
A-26— 5	2 mos.	M	57.0	3,550	+	3 days	6.0	Pneumonia ?
Friedleben 242	2 mos.	F	....	2,667	++	1 day	6.0	Cerebral edema; intestinal irritation
A-28— 590	3 mos.	F	....	.....	+++	2 days	16.0	Edema of lungs
A-24— 624	3 mos.	F	....	.....	+++	3 days	18.6	Infectious course clinically
A-20— 410	4 mos.	M	63.0	4,990	+++	2 days	20.0	
A-23— 246	5 mos.	M	63.0	.....	+++	6 days	12.0	Recurrent convulsions
A-22— 208	11 mos.	M	70.0	.....	+++	5 days	20.0	Fatty degeneration of liver
A-26— 214	11 mos.	M	75.0	.....	+++	2 days	19.4	"Cold" for 2 days
Hammar, no. 1432								
c. Infections								
A-28— 801	1 day	M	48.0	.....	+++	Life	4.0	Pneumonia
A-23— 145	1 day	M	53.0	4,820	+++	Life	30.0	Aspiration pneumonia
A-28—1573	2 days	M	46.0	.....	+++	Life	7.0	Pneumonia; birth trauma ?
A-19— 55	2 days	M	53.0	.....	+++	Life	10.0	Abscess of kidney; hepatitis
A-27—1171	4 days	M	52.0	3,000	++	3 days	9.4	Septicemia; abscess of spleen
A-25— 43	4 days	M	51.0	3,100	+++	2 days	5.0	Peritonitis; streptococcus
A-25— 165	4 days	M	50.0	2,710	+++	2 days	5.0	Pneumonia
A-18— 186	4 days	F	54.0	.....	+++	2 days	7.3	Pneumonia
A-28— 307	4 days	M	51.5	.....	+++	Life	3.3	Pneumonia
A-26— 730	5 days	F	53.0	4,450	+++	3 days	9.0	Hemorrhagic pneumonia
A-28— 980	5 days	F	54.0	.....	+++	3 days	5.0	Pneumonia
A-15— 168	5 days	M	48.0	.....	+++	1 day	6.1	Pneumonia
A-15— 306	5 days	M	48.0	.....	+++	Life	3.5	Congenital syphilis
A-24— 367	6 days	F	47.0	2,100	++	Life	3.3	Pneumonia
A-23— 506	6 days	M	50.0	3,850	+++	5 days	12.0	Empyema
Friedleben 227	6 days	M	....	2,747	++	2 days	3.6	Erysipelas
A-23— 399	7 days	M	51.0	.....	++	1 day	9.7	Omphalitis; septicemia
A-26— 23	7 days	F	51.5	.....	++	3 days	8.1	Septicemia
A-26— 473	8 days	F	50.0	3,000	+++	1 day	6.9	Meningitis
A-24— 42	9 days	F	52.0	3,135	++	3 days	3.0	Peritonitis
A-27— 91	10 days	M	52.0	.....	+++	1 day	5.4	Pneumonia
A-20— 181	10 days	M	50.0	2,875	+++	1 day	5.0	Omphalitis; peritonitis
A-27—1264	11 days	F	52.0	3,525	+++	1 day	6.6	Pneumonia; erysipelas
Friedleben 230	11 days	..	....	2,239	++	1 day	3.6	Cholerine; colitis
A-27— 935	12 days	F	52.0	3,785	++	2 days	4.8	Pneumonia; septicemia
A-24— 21	13 days	M	47.5	2,550	++	3 days	4.2	Acute pancreatitis
A-26— 906	16 days	M	52.0	2,907	++	2 days	3.0	Pneumonia; gastric ulcer from lactic acid
A-25— 144	16 days	M	49.0	2,500	+++	3 days	5.0	Erysipelas; meningitis
A-23— 722	17 days	M	52.0	3,440	+++	1 day	12.0	Pneumonia

A-27— 890	17 days	F	50.0	.....	++++	1 day	12.0	Pneumonia
A-22— 112	2½ wks.	M	46.0	2,075	+	1 day	5.0	Erysipelas
A-23— 405	19 days	F	55.0	3,300	++	1 day	4.0	Meningitis; streptococcus
A-26— 821	20 days	M	52.5	.....	++++	4 days	5.0	Hemorrhagic encephalitis
A-27— 797	3 wks.	M	46.5	.....	+	3 days	2.0	Pneumonia; pyloric stenosis
A-23— 406	22 days	F	50.0	2,255	+	6 days	4.5	Enterocolitis; septicemia; colon bacillus
A-26— 527	23 days	M	53.0	2,270	+	5 days	4.0	Peritonitis; pneumonia
A-26— 478	26 days	F	47.0	2,320	++	6 days	1.7	Erysipelas
A-26— 28	1 mo.	F	50.0	.....	++	1 day	7.1	Bronchopneumonia
A-15— 270	31 days	M	52.0	.....	+	3 days	10.0	Acute enterocolitis
A-27— 583	1 mo.	M	52.3	.....	+	2 days	9.0	Pneumonia
A-25— 970	5 wks.	M	59.0	5,710	+	5 days	11.0	Pneumonia
A-25— 928	41 days	F	....	3,200	+	5 days	6.8	Congenital syphilis
A-24— 773	6 wks.	M	47.0	2,720	++	4 days	6.0	Pneumonia
A-27— 216	6 wks.	F	56.0	4,090	+++	2 days	11.9	Rheumatic endocarditis
A-25— 206	7 wks.	M	53.0	.....	+++	2 days	10.0	Pneumonia; meningitis
A-25— 38	2 mos.	F	47.0	2,400	++	3 days	7.0	Smallpox
A-27— 880	2 mos.	M	62.0	.....	++++	4 days	20.0	Pneumonia
A-28— 694	3 mos.	M	61.0	.....	+++	5 days	5.2	Meningitis
A-22— 314	3 mos.	M	57.0	3,800	+	4 days	7.0	Pneumonia
A-27—1338	3 mos.	F	57.0	4,656	+++	3 days	28.0	Otitis media; pneumonia
A-29— 390	3 mos.	F	58.0	5,120	+++	2 days	18.0	Otitis media; pneumonia
A-25—1008	4 mos.	M	56.0	3,090	+	1 day	6.0	Pneumonia
A-28— 34	4 mos.	F	53.5	.....	++	3 days	6.0	Pneumonia
A-22— 379	5 mos.	M	61.5	4,800	+++	3 days	12.0	Peritonitis
A-27— 571	5 mos.	F	64.0	6,330	+++	3 days	17.5	Meningitis; mastoiditis
A-28— 38	5 mos.	M	63.0	5,300	++	6 days	10.0	Pneumonia; colitis
A-25— 172	6 mos.	F	60.0	.....	+++	1 day	10.0	Pneumonia; fatty degeneration of liver
A-24— 673	6 mos.	M	71.0	.....	+++	3 days	20.0	Pneumonia; tracheobronchitis
A-27— 534	6 mos.	F	63.5	.....	+++	3 days	17.0	Pneumonia
A-21— 335	6 mos.	F	....	.....	+++	4 days	15.0	Enteritis
A-27—1260	6 mos.	F	71.0	.....	+++	4 days	10.0	Pneumonia; mastoiditis; meningitis
A-26— 10	7 mos.	M	70.0	6,300	++	6 days	12.7	Pneumonia
Friedleben 264	7 mos.	M	....	5,642	++++	5 days	11.6	Intestinal catarrh
A-23— 575	8 mos.	M	73.0	.....	+++	3 days	13.3	Aspiration pneumonia; diarrhea and vomiting
A-28— 511	8 mos.	M	64.0	.....	+++	3 days	5.1	Pneumonia
Friedleben 270	8 mos.	M	....	6,036	+++	30 hrs.	10.3	Cholerine
A-24— 732	9 mos.	M	65.0	6,350	++	2 days	15.0	Pneumonia; rickets
A- 9— 941	9 mos.	M	64.0	.....	+++	3 days	25.0	Poliomyelitis
A-24— 73	10 mos.	F	60.0	5,850	+++	1 day	22.0	Pneumonia
A-29—1516	10 mos.	M	71.0	.....	+++	2 days	25.0	Pneumonia
A-26— 290	10 mos.	F	69.5	.....	+++	4 days	13.0	Pneumonia
A-16— 405	11 mos.	M	74.0	.....	+++	1 day	36.0	Meningitis
A-26— 644	11 mos.	F	68.5	.....	++	2 days	16.5	Meningitis
A-21— 342	11½ mos.	M	81.0	13,590	++++	2 days	60.0	Meningitis

Hammar, nos. 1349, 904, 1160, 795, 1244, 1676, 1549, 1112, 864, 861, 868, 1814, 785, 1821, 1584, 876 and 1822
von Mettenheimer, nos. 26 and 14

TABLE 1.—*Thymus Weights Arranged According to Age, Duration of Illness and Cause of Death—Continued*

Source and Number	Age	Sex	Height of Body, Cm.	Weight of Body, Gm.	Nutritional Rank	Duration of Illness	Weight of Thymus, Gm.	Cause of Death
2. 1 Day to 1 Year—B. Ill One to Seven Days—Continued—d. Congenital Defects								
A-21— 38	1 day	F	53.5	.....	+	Life	5.0	Atresia of small intestine
A-28—1464	2 days	M	50.0	2,735	++	Life	15.0	Cardiac defect
A-25— 526	2 days	M	52.0	3,200	+++	Life	18.0	Cardiac defect; birth trauma
A-25— 167	2 days	M	48.0	2,470	+++	Life	10.0	Hydrocephalus
A-24— 396	3 days	F	55.0	.....	++	2 days	8.0	Atresia of duodenum
A-27— 815	3 days	M	50.0	3,210	++	Life	7.0	Aplasia of rectum
A-17— 238	3 days	M	55.0	.....	+++	Life	10.0	Stenosis of larynx
A-27— 152	3 days	M	53.0	3,200	+	Life	3.5	Defect of kidney; peritonitis; colon bacillus
A-23— 576	4 days	F	45.0	2,270	++	Life	5.2	Cardiac defect
A-29—1868	4 days	F	48.0	3,630	++	Life	9.0	Spina bifida; meningitis
A-23— 134	4 days	M	45.0	3,800	+++	Life	11.5	Laryngeal stridor
A-28— 6	4 days	F	51.0	.....	+++	Life	11.0	Cardiac defect
A-26— 669	5 days	F	....	2,860	++	Life	7.3	Multiple defects
A-22— 283	5 days	F	50.0	.....	+++	Life	10.0	Stenosis of trachea
A-26— 42	5 days	M	51.0	3,400	+++	Life	5.0	Tracheobronchial fistula
A-24— 352	7 days	F	47.0	1,975	++	1 day	6.0	Cardiac defect; birth trauma
A-27— 380	8 days	F	52.0	3,040	++	3 days	7.0	Cardiac defect; pneumonia
A-20— 240	2 mos.	M	55.0	3,000	+++	5 days	12.0	Hemangioma of larynx
A-28—1189	3 mos.	M	61.0	4,470	++	1 day	7.5	Multiple defects; pneumonia
A-22— 98	9 mos.	F	....	.....	+++	1 day	15.0	Cardiac defects; pneumonia
Hammar, nos. 991 and 1420								
von Mettenheimer, no. 55								
e. Miscellaneous Causes								
A-20— 3	2 days	F	47.0	1,740	++	Life	5.0	Maternal toxemia
A-20— 350	2 days	M	51.5	2,960	++	Life	6.0	Hemorrhagic disease
A-21— 378	2 days	M	49.0	.....	+++	1 day	8.5	Hemorrhage from duodenal ulcer
A-23— 301	2 days	F	51.0	3,325	+++	1 day	12.0	Hemorrhage from duodenal ulcer
A-23— 663	2 days	M	51.5	3,000	+++	Life	10.0	Hemolytic jaundice
A-28— 859	2 days	M	51.0	3,375	+++	Life	11.0	Splenomegaly
A-16— 351	3 days	M	49.5	.....	+	Life	9.0	Hemorrhagic disease
A-27—1101	3 days	F	50.0	.....	++	2 days	6.4	Hemorrhagic disease; birth trauma
A-18— 106	3 days	F	51.0	.....	+++	1 day	18.0	Melena neonatorum
A-22— 274	3 days	F	51.0	.....	+++	Life	10.0	Hemorrhagic disease
A-27— 357	3 days	M	50.3	2,500	+++	2 days	9.2	Hemorrhage from duodenal ulcer
A-27— 592	3 days	F	50.0	3,130	+++	Life	3.9	Bowel obstruction; peritonitis
A-25— 46	3 days	M	52.0	.....	+++	Life	6.5	Hemorrhagic disease; birth trauma
A-26— 288	3½ days	F	48.0	2,700	+++	1 day	11.0	Hemorrhagic disease
A-26— 323	3½ days	M	51.0	2,800	+++	Life	6.8	Splenomegaly
A-26— 762	4 days	F	46.0	2,600	+	Life	7.4	Intestinal obstruction
A-21— 459	4 days	M	53.0	3,850	+++	Life	11.0	Hemorrhagic disease
A-18— 179	5 days	F	52.0	2,945	++	Life	3.3	Hemorrhagic disease
A-22— 16	5 days	M	45.0	2,615	+++	3 days	6.0	Hemorrhagic disease; birth trauma
A-23— 591	6 days	F	53.0	3,070	+++	1 day	6.8	Rectal hemorrhage; birth trauma
A-25— 92	7 days	M	50.0	3,205	+++	4 days	6.0	Hemorrhagic disease; birth trauma
A-28— 208	2½ wks.	F	58.5	.....	+++	1 day	12.5	Purpura hemorrhagica
A-28—1538	3 mos.	M	55.0	.....	+++	1 day	12.0	Cardiac enlargement
Friedleben 252	3½ mos.	M	....	6,489	+++	4 days	11.8	Intussusception; colitis
A-22— 57	4 mos.	F	....	.....	+++	3 days	22.0	Idiopathic cardiac enlargement
	4½ mos.	M	66.0	.....	+++	4 days	8.5	Intussusception; peritonitis
							25.0	Intussusception; ulcer in colon

A-28—1538	3 mos.	M	55.0	.....	+++	1 day	12.0	Cardiac enlargement
Friedleben 252	3½ mos.	M	....	6,480	+++	4 days	11.8	Intussusception; colitis
A-22— 57	4 mos.	F	....	.....	+++	3 days	22.0	Idiopathic cardiac enlargement
A-26—1104	4½ mos.	M	66.0	.....	+++	4 days	8.5	Intussusception; peritonitis
A-21— 375	6 mos.	M	53.0	5,400	+++	1 day	35.0	Intussusception; ulcer in colon
A-26—1024	6 mos.	M	69.0	.....	++++	3 days	18.0	Intussusception
A-28— 835	8 mos.	M	68.0	.....	+++	2 days	29.0	Intussusception
Hammar, nos. 1138, 977, 1532, 1015, 1673, 1206, 1789, 1669, 1380, 1556, 1589 and 957								
O. Ill One Week or More——a. Accidents								
A-25— 490	8 days	M	53.0	3,150	++	Life	5.5	Birth trauma
A-28—1405	12 days	M	51.0	.....	+++	Life	10.0	Birth trauma
A-27— 927	13 days	M	50.0	1,420	+	Life	2.6	Cerebral hemorrhage; aspiration of milk
A-25— 577	22 days	M	48.0	2,000	+	Life	2.0	Birth trauma; aspiration
A-16— 296	1 mo.	M	55.0	2,750	+	Life	7.0	Old fracture of skull
Hammar, no. 1431								
b. Undetermined Causes								
A-24— 470	9 days	F	46.0	1,520	+	Life	1.5	
Friedleben 251	11 days	..	....	1,553	+	9 days	1.7	Hyperemia of brain
A-25— 653	12 days	F	45.6	1,540	+	Life	2.5	Birth trauma ?
A-29—1009	2 wks.	F	50.0	2,100	+	Life	3.0	
A-26— 101	15 days	F	45.0	1,500	+	Life	1.5	
A-15— 72	15 days	M	45.0	2,260	+	10 days	4.8	
A-28— 266	16 days	M	45.5	1,790	++	Life	2.0	
A-24— 68	16 days	M	55.0	.....	+++	Life	20.0	Symptoms of ileocolitis
A-24— 449	19 days	F	46.0	1,475	+	Life	1.1	
A-28— 614	20 days	F	....	.....	+++	Found dead 15 days	14.0	Edema of lungs
A-24— 795	22 days	F	45.5	1,960	+	Life	1.5	
A-28— 130	25 days	M	49.0	2,300	+	Life	10.6	Inanition
A-28— 430	4 wks.	F	47.0	.....	+	3 wks.	2.8	
A-18— 196	5 wks.	M	50.0	.....	++	1 wk.	9.0	Cough; "cold"
A-25— 239	5 wks.	M	49.0	3,000	++	Life	10.0	Pneumonia ?
A-26— 132	1½ mos.	F	47.0	2,200	+	7 days	4.0	Aspiration ?
A-27— 619	2 mos.	F	53.0	.....	++	1 wk.	1.5	Temperature 107 F.
A-22— 58	4 mos.	M	65.0	5,470	+++	2 wks.	12.0	
Friedleben 256	5½ mos.	F	....	3,310	+	2 mos.	1.9	Cerebral edema; anemia
A-27—1216	7 mos.	M	68.0	6,970	+++	1 wk.	28.0	
A-28— 514	8 mos.	M	72.0	7,711	+++	9 days	11.8	Pulmonary edema; fatty degeneration of liver; temperature 105 F.
A-26— 885	11 mos.	..	68.0	.....	++++	8 days	8.0	Diarrhea and vomiting; fatty degeneration of liver
Hammar, nos. 973, 1534, 741, 1511 and 906								
c. Infections								
A-24— 117	8 days	F	47.0	1,940	++	Life	4.0	Pneumonia
A-23— 400	9 days	M	52.5	2,300	+	Life	8.2	Meningitis; colon bacillus
A-25— 154	9 days	F	46.5	1,780	+	8 days	3.7	Pneumonia; birth trauma
A-16— 245	9 days	F	53.0	.....	+++	8 days	4.5	Impetigo
Friedleben 229	9 days	..	....	2,294	++	Life	2.3	Pulmonary abscess
A-12— 151	10 days	M	53.5	.....	+	8 days	6.0	Acute pemphigus
A-24— 281	10 days	F	49.0	2,490	++	8 days	2.0	Erysipelas
A-22— 124	12 days	F	....	2,000	++	8 days	2.0	Pneumonia; inanition
A-22— 158	12 days	M	57.0	2,370	+	8 days	3.0	Conjunctivitis; gonococcus; malnutrition
A-28— 696	12 days	M	46.0	1,570	+	8 days	2.0	Pneumonia; malnutrition
A-26— 479	13 days	F	48.0	2,160	++	10 days	6.0	Enteritis; temperature 102 F.
A-20— 116	14 days	F	45.0	.....	++	Life	3.0	Congenital syphilis

TABLE 1.—*Thymus Weights Arranged According to Age, Duration of Illness and Cause of Death—Continued*

Source and Number	Age	Sex	Height of Body, Cm.	Weight of Body, Gm.	Nutritional Rank	Duration of Illness	Weight of Thymus, Gm.	Cause of Death
2. 1 Day to 1 Year—C. Ill One Week or More—c. Infections—Continued								
A-26— 287	14 days	F	50.0	2,000	+	12 days	2.2	Omphalitis; streptococcus
Friedleben 232	14 days	..	....	3,171	++	7 days	5.6	Thrush
A-22— 79	2 wks.	M	45.0	1,930	+	Life	6.0	Pneumonia
A-22— 232	2 wks.	M	47.0	1,720	+	Life	1.5	Pneumonia; malnutrition
A-28— 610	2 wks.	M	48.0	.....	+	Life†	2.2	Pneumonia; inanition
A-25— 263	15 days	M	50.5	2,605	+	Life	5.2	Aspiration; pneumonia
A-27— 463	15 days	M	52.0	.....	+	Life	3.0	Pneumonia; birth trauma
Friedleben 233	15 days	..	....	2,301	++	8 days	6.2	Enteritis
A-23— 567	16 days	F	45.0	2,580	+	11 days	7.5	Peritonitis; psoas abscess
A-25— 52	17 days	F	45.0	1,500	++	Life	5.5	Pneumonia
A-24— 52	18 days	M	55.0	3,475	++	7 days	4.2	Omphalitis
A-24— 371	18 days	M	45.5	1,720	++	Life	4.0	Pneumonia
A-25— 668	18 days	M	47.1	1,850	+	15 days	2.0	Ileocolitis
A-17— 61	1 mo.	M	....	3,040	++	12 days	5.0	Omphalitis
A-23— 59	1 mo.	M	47.0	2,650	+	Life	12.0	Pneumonia
Friedleben 234	18 days	..	....	1,969	+	10 days	2.6	Cholerine; pneumonia
A-23— 517	21 days	M	56.5	.....	+	10 days	6.0	Peritonitis
A-22— 19	3 wks.	F	46.0	2,005	+	2½ wks.	3.0	Congenital syphilis
A-24— 546	3 wks.	M	53.0	.....	++	Life	3.0	Congenital syphilis
A-26—1140	3 wks.	M	52.0	.....	++	1 wk.†	8.0	Pemphigus; septicemia
A-28— 711	3 wks.	M	52.0	.....	++	2 wks.†	2.8	Pyemia
A-29—1551	3 wks.	M	54.0	.....	+	1 wk.	4.0	Peritonitis; pneumonia; mastoiditis
A-25— 649	28 days	F	52.0	.....	+	Life	6.0	Pneumonia
A-27— 522	4 wks.	F	56.0	.....	+	1 wk.	3.0	Pneumonia; mastoiditis
A-27— 851	4 wks.	F	53.0	.....	+	2 wks.	4.0	Pneumonia
A-27— 567	1 mo.	M	51.5	.....	++	2 wks.	6.7	Omphalitis
A-29— 90	5 wks.	M	52.0	.....	+	7 days	2.5	Pneumonia; endocarditis
Friedleben 238	5 wks.	..	....	2,159	+	4 wks.	0.8	Caries of vertebrae
A-16— 323	6 wks.	M	56.0	.....	+	Life†	7.6	Inanition; acute colitis
A-22— 166	6 wks.	M	56.0	2,600	+	Life	3.3	Congenital syphilis; pneumonia
Friedleben 239	6 wks.	F	....	2,806	++	3 wks.	4.3	Enterocolitis
A-24— 237	1½ mos.	M	50.0	2,280	+	2 wks.	4.4	Pneumonia; malnutrition
A-28— 538	1½ mos.	F	50.0	2,067	+	Life	2.0	Pneumonia
A-25— 654	7 wks.	M	54.0	3,800	++	4 wks.	5.0	Congenital syphilis
A-28— 252	7 wks.	F	54.5	2,710	+	Life†	8.0	Otitis media; pneumonia
A-85— 327	1 mo. 28 days	M	52.5	3,295	++	Life, 2 wks.	8.0	Pneumonia
A-24— 804	2 mos.	M	60.0	4,400	+	Life	2.0	Pneumonia; malnutrition
A-25— 491	2 mos.	F	53.0	2,700	+	Life	8.5	Pneumonia; malnutrition
A-25— 202	2 mos.	M	52.0	.....	+	16 days	4.0	Ischiorectal abscess; pneumonia; peritonitis
A-26— 513	2 mos.	M	60.0	2,670	+	6 wks.	4.0	Scarlet fever; mastoiditis
Friedleben 241	2 mos.	M	....	2,170	++	2 wks.	1.0	Enteritis follicularis
Friedleben 243	2 mos.	F	....	3,105	++	3 wks.	1.0	Peritonitis; pyemia
A-27— 253	2½ mos.	M	58.0	.....	+	Life†	8.0	Pneumonia
A-27— 529	2½ mos.	F	48.5	2,750	++	2 wks.	5.0	Pneumonia
A-27— 538	2½ mos.	F	49.5	2,730	+	6 wks.	3.0	Pneumonia; mastoiditis
A-27— 333	2½ mos.	M	54.0	4,400	++	Life	6.0	Pneumonia; congenital syphilis
A-27— 334	2½ mos.	M	54.0	4,400	++	14 days	3.9	Tuberculosis universalis

A-27— 333	2½ mos.	M	54.0	4,400	++	Life	6.0	Pneumonia; congenital syphilis
Friedleben 245	2½ mos.	M	....	3,456	+	14 days	3.9	Tuberculosis universalis
Friedleben 246	2½ mos.	F	....	3,248	+	5 wks.	7.2	Tuberculous cervical adenitis
Friedleben 247	2½ mos.	M	....	3,668	+	3½ wks.	1.8	Suppurative ependymitis; hydrocephalus
A-23— 117	12 wks.	F	58.0	.....	+	11½ wks.	2.0	Pneumonia
A-28— 809	3 mos.	F	55.0	.....	+	1 wk.	4.0	Pneumonia
A-26— 561	3 mos.	M	56.0	4,400	+++	7 days	9.0	Pneumonia
A-27— 217	3 mos.	F	66.0	.....	+++	3 wks.	10.2	Pneumonia
A-26— 831	3 mos.	M	56.0	3,650	++	Life†	14.0	Pneumonia; malnutrition
A-26—1084	3 mos.	M	61.0	4,500	++	8 days	5.0	Meningitis; streptococcus
A-27— 311	3 mos.	F	50.0	2,650	+	2 wks.	9.5	Otitis media; pneumonia
Friedleben 248	3 mos.	F	....	3,413	++	3 wks.	1.6	Pertussis
Friedleben 249	3 mos.	M	....	2,689	++	6 wks.	4.4	Enteritis
Friedleben 250	3 mos.	M	....	4,816	+++	8 days	8.2	Pneumonia
A-27—1038	3½ mos.	M	59.0	3,875	+	2½ mos.	2.6	Congenital syphilis; pneumonia
A-22— 640	3¾ mos.	M	57.5	3,670	+	1 mo.	3.0	Otitis media; pneumonia
A-23— 361	4 mos.	F	65.0	.....	++	3 wks.	7.0	Miliary tuberculosis
A-24— 472	4 mos.	M	62.0	4,190	+	Life	4.0	Encephalomalacia; abscess on buttock
A-26— 595	4 mos.	M	45.0	.....	++	Life†	6.0	Pneumonia
A-26— 845	4 mos.	F	62.0	4,350	++	1 mo.	8.5	Pneumonia
A-26—1011	4 mos.	M	66.0	6,350	++	1 mo.	5.2	Pneumonia; sinusitis
A-28— 478	4 mos.	M	57.0	.....	+	1 mo.	3.4	Pneumonia
A-23— 160	4 mos.	F	60.0	.....	+++	11 days	4.0	Pneumonia
Friedleben 253	4 mos.	F	....	3,566	+	14 days	3.6	Miliary tuberculosis
A-25— 176	4½ mos.	M	66.0	7,711	+++	25 days	8.0	Pneumonia
Friedelben 254	4½ mos.	F	....	4,090	+	7 wks.	2.3	Tuberculosis universalis
A-24— 196	4¾ mos.	M	61.0	5,700	+++	7 days	15.5	Pneumonia
A-23— 682	5 mos.	M	64.0	5,760	+++	10 days	15.0	Meningitis; pneumonia
A-26— 419	5 mos.	F	61.0	.....	+++	2 wks.	5.0	Peritonitis; streptococcus
A-28— 634	5 mos.	F	64.0	5,360	+++	1 wk.	11.0	Peritonitis; pneumonia
A-15— 277	5 mos.	M	56.0	.....	++	5 mos.	2.0	Congenital syphilis; acute enteritis
A-27— 424	5 mos.	F	62.0	5,700	++	4 mos.	3.0	Recurrent sinusitis; meningitis
A-27— 481	5 mos.	M	64.5	3,890	++	4 mos.	10.0	Syphilitic meningitis
A-27— 736	5 mos.	M	69.0	7,175	++	7 days	4.1	Pneumonia; meningitis
A-27—1263	5 mos.	F	59.0	.....	++	4 mos.	2.0	Mastoiditis; sinus thrombosis
A-28— 433	5 mos.	F	57.0	3,550	+	4 mos.	3.0	Pneumonia
A-28— 607	5 mos.	M	60.0	5,128	++	3 wks.	8.0	Pneumonia; peritonitis
A-22— 144	5½ mos.	F	64.0	4,700	+	2 wks.	5.0	Multiple abscesses
A-22— 170	6 mos.	M	64.0	5,120	++	5 wks.	5.8	Peritonitis
A-26— 970	6 mos.	F	56.0	3,120	+	Life	8.0	Pneumonia; malnutrition
A-22— 130	6 mos.	F	66.0	10,870	+++	2 wks.	5.0	Pneumonia
A-24— 671	6 mos.	F	65.0	.....	+++	2 wks.	15.0	Pneumonia
Friedleben 259	6 mos.	F	....	4,794	++	3 mos.	2.5	Tuberculous adenitis
Friedleben 260	6 mos.	F	....	2,843	+	2 mos.	2.5	Pulmonary and intestinal tuberculosis
A-25— 122	6½ mos.	F	65.0	.....	++++	7 days	27.0	Pneumonia; meningitis
Friedleben 261	6 mos. 20 days	M	....	3,975	+	Many mos.	2.9	Tuberculous adenitis
Friedleben 262	6 mos. 21 days	F	....	2,579	+	Many mos.	1.8	Chronic follicular enteritis
A-27— 650	7 mos.	M	63.0	6,080	+++	8 days	10.9	Pneumonia
A-17— 48	7 mos.	F	65.0	.....	+	3 wks.	5.0	Pneumonia; otitis media
A-24— 473	7 mos.	M	67.0	4,820	++	17 days	5.0	Pneumonia; retropharyngeal abscess
A-25— 34	7 mos.	M	70.0	.....	+	6 wks.	10.0	Pneumonia
A-27—1261	7 mos.	M	58.0	.....	+	Life	3.0	Pneumonia; malnutrition
Friedleben 263	7 mos.	F	....	4,735	+	5 wks.	2.0	Empyema; pneumonia; enteritis

TABLE 1.—*Thymus Weights Arranged According to Age, Duration of Illness and Cause of Death—Continued*

Source and Number	Age	Sex	Height of Body, Cm.	Weight of Body, Gm.	Nutritional Rank	Duration of Illness	Weight of Thymus, Gm.	Cause of Death
2. 1 Day to 1 Year—C. Ill One Week or More—c. Infections—Continued								
Friedleben 265	7 mos.	F	....	5,210	++	10 days	4.1	Pertussis; enteritis
Friedleben 266	7 mos. 25 days	F	....	9,653	+++	14 days	9.9	Tuberculosis; acute bronchitis
A-26— 590	8 mos.	M	71.0	.....	++	10 days	3.3	Pneumonia; pulmonary abscess
A-28— 595	8 mos.	F	57.0	4,015	++	Life	7.0	Pneumonia
A-25— 128	8 mos.	F	61.0	.....	+++	1 wk.	8.0	Tuberculous meningitis
Friedleben 267	8 mos.	F	....	3,040	+	8 mos.	0.4	Tuberculosis universalis
Friedleben 268	8 mos.	F	....	3,040	+	Many mos.	0.4	Tuberculosis universalis
Friedleben 271	8 mos.	M	....	5,977	++	14 days	8.1	Measles; cerebral irritation
A-25— 903	9 mos.	F	68.0	.....	++	5 mos.	7.0	Pneumonia; pulmonary abscess
Friedleben 275	9 mos.	M	....	5,744	++	28 days	2.8	Pneumonia; enteritis
A-25— 108	10 mos.	M	74.0	.....	++	2 wks.	8.0	Tuberculosis
A-26—1000	10 mos.	M	68.0	6,385	++	Few mos.†	5.0	Pneumonia
A-18— 81	10 mos.	F	64.0	.....	+++	3 mos.	10.2	Empyema; congenital syphilis
Friedleben 279	10 mos.	F	....	3,668	+	Many mos.	1.5	Tuberculosis universalis
A-27— 118	11 mos.	M	73.0	.....	+++	1 wk.	9.7	Meningitis
Friedleben 280	11 mos.	M	....	6,836	++	14 days	3.7	Measles; angina of larynx
Hammar, nos. 1012, 1046, 1084, 1044, 1345, 1733, 1601, 1305, 67, 1342, 1510, 990, 1040, 1108, 1261, 986, 1434, 798, 1067, 1038, 1595, 1098, 1165, 1566, 1662, 1709, 1039, 1024, 934, 1551, 1327, 1274, 1559, 1113, 1037, 870, 1561, 1716, 1017, 1030 and 1638								
von Mettenheimer, no. 49								
d. Congenital Defects								
Friedleben 228	9 days	F	....	2,338	++	Life	1.5	Spina bifida; meningitis
A-25— 67	10 days	M	47.0	2,310	+	Life	1.8	Spina bifida; meningitis
A-28—1717	10 days	F	45.0	1,650	++	Life	2.4	Cardiac defect
A-24— 403	12 days	M	46.0	1,580	+	12 days	0.5	Tracheo-esophageal fistula
A-24— 816	15 days	F	46.0	2,500	++	Life	3.5	Spina bifida; meningitis; colon bacillus
A-28— 451	3 wks.	M	52.0	.....	+	18 days	1.2	Stenosis of hepatic duct
A-26— 811	1 mo.	F	56.0	3,700	+++	Life	4.5	Infected meningocele
A-26— 663	2 mos.	M	58.0	4,250	+++	Life	5.4	Defects of heart and mandible
A-26—1036	2 mos.	F	54.0	.....	+	Life	6.8	Cardiac defect
A-26— 127	2 mos.	M	50.0	2,300	+	Life	1.2	Cleft palate; abscess of lung
A-26— 465	2 mos.	M	55.0	3,635	+	Life	5.2	Cleft palate; pneumonia
A-28— 474	2 mos.	M	51.0	.....	++	7 wks.	4.2	Defect of kidney; pneumonia
A-26— 451	9 wks.	M	....	.....	+++	2 wks.	4.3	Cleft palate; pneumonia
A-15— 153	2 mos. 9 days	M	54.0	.....	+	9 days	9.5	Cardiac defect; pneumonia
A-27— 915	3 mos.	M	58.0	4,935	+++	1 wk.	7.2	Cardiac defects
A-26—1003	3 mos.	M	57.0	3,500	+	Life	2.4	Cleft palate; pneumonia
A-25— 320	3½ mos.	M	64.0	4,300	++	2 wks.	18.0	Cardiac defects
A-22— 326	3½ mos.	F	61.0	3,720	+	Life	9.0	Cleft palate; pneumonia
A-26— 511	3½ mos.	M	61.0	.....	++	3 wks.†	14.5	Cleft palate; pneumonia
A-25— 644	5 mos.	F	93.0	.....	+	Life	2.0	Spina bifida; meningitis
A-24— 388	6 mos.	M	55.0	3,400	+	1 wk.	4.0	Cardiac defect; malnutrition
A-23— 616	8 mos.	F	68.0	12,200	++++	Life, 3 wks.	8.2	Spina bifida; ileocolitis
A-24— 820	8 mos.	F	67.0	6,620	+	8 mos.	1.0	Spina bifida; hydrocephalis

A-24— 388	6 mos.	M	55.0	3,400	+	1 wk.	4.0	Cardiac defect; malnutrition
A-23— 616	8 mos.	F	68.0	12,200	++++	Life, 3 wks.	8.2	Spina bifida; ileocolitis
A-24— 820	8 mos.	F	67.0	6,620	+	8 mos.	1.0	Spina bifida; hydrocephalis
Hammar, nos. 1592, 1016 and 1557								
e. Miscellaneous Causes								
A-25— 235	11 days	M	50.3	2,930	+++	10 days	8.0	Splenomegaly; severe anemia
A-26— 343	15 days	M	52.0	.....	++	12 days	3.8	Splenomegaly
A-24— 691	20 days	M	51.0	2,700	+	16 days	2.0	Chylothorax
Friedleben 235	20 days	..	....	2,757	++	14 days	15.1	Icterus gravis
A-27— 672	3 wks.	F	53.0	.....	+	8 days	8.0	Hemolytic jaundice
A-28— 527	3 wks.	F	50.0	2,360	+	3 days	6.0	Blood in cerebral ventricles
A-15— 180	5 wks.	F	50.0	2,375	+	Life†	5.0	Malnutrition
A-23— 572	6 wks.	M	50.0	2,530	+	3 wks.	3.9	Malnutrition; aspiration of gastric contents
A-27— 928	6 wks.	M	52.0	1,640	+	3 wks.	2.2	Pyloric stenosis; postoperative peritonitis
A-27—1348	6 wks.	M	52.0	.....	+	2 wks.	4.0	Pyloric stenosis; postoperative peritonitis
A-23— 60	7 wks.	M	....	.....	+	4 wks.	6.0	Pyloric stenosis; died after operation
A-28— 977	8 wks.	F	54.0	2,700	+	Life	4.0	Intestinal obstruction
A-27— 241	2 mos.	F	55.0	4,000	++	6 wks.	14.0	Aspiration of blood from throat
A-18— 133	10 wks.	M	45.0	.....	+	Life	3.0	Marasmus
A-23— 607	2½ mos.	M	55.5	2,190	+	2 wks.	1.0	Pyloric stenosis; died following operation
A-24— 32	2½ mos.	M	50.0	2,710	+	Life	2.5	Malnutrition
A-20—1593	2½ mos.	F	....	.....	+	3 wks.	0.9	Pylorospasm; pneumonia
A-28—1020	2½ mos.	F	56.0	.....	++	2 mos.	11.3	Pyloric stenosis
A-24— 518	2⅔ mos.	M	53.0	2,870	+	2 mos.	5.5	Pyloric stenosis
A-24— 313	3 mos.	F	54.0	2,915	++	Life†	9.1	Inanition
A-24— 640	3 mos.	M	59.0	3,685	+	Life†	11.0	Malnutrition
A-27— 913	3 mos.	F	52.0	.....	+	Life	2.2	Malnutrition; aspiration of milk
A-26— 153	3 mos.	F	62.0	4,380	++	6 wks.	11.0	Cardiac enlargement; myocardial fibrosis
A-16— 210	3¼ mos.	M	51.0	.....	+	2½ mos.	3.0	Pyloric stenosis
A-15— 121	4 mos.	F	56.0	.....	+	1 mo.†	7.8	Malnutrition
A-15— 278	4 mos.	M	61.5	.....	+	Life	6.5	Malnutrition
A-25— 657	4 mos.	M	55.5	.....	+++	Life; few days	30.0	Hydrocephalus; ulcers in ileum
A-23— 630	4½ mos.	M	50.0	3,500	+	Life	1.0	Malnutrition; furunculosis
A-20— 366	5 mos.	M	70.0	.....	++	5 mos.	25.0	Hydrocephalus
A-29—1111	5 mos.	F	58.0	4,795	+	Life	15.0	Little's disease; malnutrition
A-17— 224	5½ mos.	M	....	.....	+	Life	7.0	Marasmus; otitis media
A-23— 724	6 mos.	M	57.0	3,450	+	Life	8.0	Malnutrition
Friedleben 258	6 mos.	M	....	3,610	+	Life	5.3	Hydrocephalus
Friedleben 257	6 mos.	M	....	4,063	++	8 days	9.0	Rickets; chronic bronchitis; pneumonia
A-28— 699	6 mos.	F	52.0	.....	+	Life	3.2	Hydrocephalus; pneumonia
A-21— 193	6½ mos.	M	47.0	2,130	+	Life	2.0	Inanition
A-16— 414	7 mos.	F	56.0	2,850	+	1 mo.†	4.8	Malnutrition
A-23— 195	7 mos.	M	68.0	.....	+	10 wks.	5.0	Athrepsia
A-27—1323	7 mos.	M	58.0	3,800	+	3 mos.	4.0	Cirrhosis of liver; peritonitis
A-21— 447	8 mos.	M	64.0	3,145	+	8 mos.	1.7	Malnutrition
A-26—1103	8 mos.	F	67.0	.....	+	2 wks.	4.0	Malnutrition from persistent vomiting
A-27— 747	8 mos.	M	69.0	.....	+++	12 days	4.6	Acidosis
Friedleben 269	8 mos.	M	....	4,786	++	3 mos.	7.3	Rickets; pneumonia
Friedleben 272	8 mos.	F	....	3,807	++	Many mos.	5.7	Rickets; pneumonia
Friedleben 276	9 mos. 13 days	M	....	3,778	+	Many mos.	0.9	Rickets; pneumonia; severe diarrhea
Hammar, nos. 1031, 1517, 1539, 1029, 1547, 998, 1443, 1022, 1698, 1314 and 1640								
f. Exophthalmic Goiter and Leukemia								
A-20— 193	2½ mos.	M	60.0	.....	+++	2 wks.	15.0	Acute lymphatic leukemia

TABLE 1.—*Thymus Weights Arranged According to Age, Duration of Illness and Cause of Death—Continued*

Source and Number	Age	Sex	Height of Body, Cm.	Weight of Body, Gm.	Nutritional Rank	Duration of Illness	Weight of Thymus, Gm.	Cause of Death
3. 1 to 3 Years—A. Ill Less Than Twenty-Four Hours—a. Accidents								
A-27— 185	1 yr.	M	74.0	7,813	+++	30 mins.	38.0	Bean in trachea
A-19— 226	13 mos.	M	76.0	12,230	+++	Found dead	17.0	Carbon monoxide poisoning
A-19— 137	15 mos.	M	82.0	.....	+++	14 hrs.	23.0	Phosphorus poisoning; chewed a "percussion cap"
A-27—1009	18 mos.	M	86.0	12,275	+++	4 hrs.	30.0	Foreign body in trachea
A-28— 678	18 mos.	M	79.0	9,740	+++	6 hrs.	55.0	Edema of glottis from soap powder
A-28— 86	20 mos.	M	80.0	.....	+++	Few mins.	35.0	Fracture of skull; automobile
A-20— 199	2 yrs.	F	89.0	.....	+++	15 mins.	35.0	Fracture of skull; automobile
A-20— 288	2 yrs.	F	89.5	.....	+++	Sudden death	20.0	Electrocution
A-19— 63	2¼ yrs.	M	82.0	.....	+++	1 hr.	15.0	Strychnine poisoning
Friedleben 301	2½ yrs.	M	....	.....	+++	3 hrs.	7.0	Phosphorus poisoning
Hammar, nos. 943, 721, 1087, 1450, 624, 758 and 918								
b. Undetermined Causes								
A-20— 349	1 yr.	F	68.6	.....	+++	Found dead	21.0	
A-26— 457	20 mos.	M	70.0	.....	++	6 hrs.	18.0	Convulsions; temperature 102 F.
A-25— 302	2 yrs.	F	83.3	.....	+++	4 hrs.; sudden death	31.0	Swallowed a tack; necropsy negative
Hammar, nos. 1445, 997, 939, 971, 431 and 1723								
c. Infections								
A-25— 948	1 yr.	M	....	7,910	++++	Sudden death	40.0	Pneumonia; died during circumcision
A-26— 37	1 yr.	M	78.7	.....	++++	Found dead	14.9	Pneumonia
A-16— 316	14 mos.	F	72.0	.....	+++	4 hrs.	25.0	Encephalitis hemorrhagica
A-21— 441	1½ yrs.	M	80.0	11,325	+++	12 hrs.	25.0	Pneumonia
A-12— 29	2 yrs. 5 mos.	F	93.0	.....	+++	18 hrs.	57.0	Meningitis; meningococcus
Hammar, no. 974								
d. Congenital Defects								
A-28— 286	2 yrs.	M	86.0	.....	+++	Few hrs.	23.0	Hemorrhage following operation on cleft palate
e. Miscellaneous Causes								
Friedleben 299	2 yrs. 3 mos.	M	....	9,003	+++	Sudden death	22.3	Acute hydrocephalus; hypertrophy of left cardiac ventricle
Friedleben 302	2 yrs. 7 mos.	M	....	10,084	+++	20 hrs.	23.7	Intussusception
Hammar, nos. 928 and 1603								
B. Ill from One to Seven Days—a. Accidents								
A-21— 553	14 mos.	M	81.0	.....	+++	3 days	6.0	Foreign body in lung; pneumonia
A-22— 256	14 mos.	F	75.0	.....	+++	3 days	27.0	Second degree burn
A-15— 203	18 mos.	F	80.0	.....	+++	3 days	18.5	Foreign body in lung; pneumonia
A-10— 69	1½ yrs.	F	82.0	.....	+++	1 day	28.0	Subdural hemorrhage
A-29—1508	1½ yrs.	F	80.0	.....	+++	1 day	12.0	Second degree burn
A-27— 937	2 yrs.	M	87.0	.....	+++	3 days	12.0	Fracture of skull (struck by swing); meningitis
Hammar, nos. 1830 and 1397								
b. Undetermined Causes								
A-22— 272	15 mos.	F	74.5	.....	+++	2 days	13.0	Bronchitis

Hammar, nos. 1890 and 1397								Fracture of skull (struck by swing); meningitis

b. Undetermined Causes

A-22— 272	15 mos.	F	74.5	.....	+++	2 days	13.0	Bronchitis
A-28— 222	16 mos.	M	83.0	13,608	+++	2 days	15.0	Convulsions; fever
A-24— 56	17 mos.	M	82.0	.....	++++	2 days	35.0	Diarrhea
Friedleben 294	1 yr. 7½ mos.	M	....	.....	+++	1 day	20.0	Indigestion; convulsions
A-24— 107	22 mos.	F	87.5	.....	++++	1 day	30.0	
A-24— 157	2 yrs.	M	74.0	.....	++	2 days	9.8	Rash; temperature 106.5 F.; fatty degeneration of liver

c. Infections

A-23— 495	1 yr.	M	74.0	.....	+++	2 days	30.0	Laryngeal diphtheria
A-25— 705	13 mos.	M	80.0	.....	+++	5 days	15.0	Poliomyelitis
A-28— 268	18 mos.	F	72.0	.....	++	6 days	6.0	Congenital syphilis; bronchitis
A-19— 210	20 mos.	M	84.0	.....	+++	4 days	6.0	Meningitis
Friedleben 295	1 yr. 8 mos.	M	....	.....	+++	6 days	15.5	Laryngitis exudativa
A-24— 102	21 mos.	F	90.0	.....	+++	3 days	15.0	Septicemia; streptococcus
A-27— 321	2 yrs.	M	93.0	.....	+++	3 days	15.0	Meningitis
A-26— 624	2 yrs.	F	80.0	.....	+++	1 day	20.0	Septicemia; streptococcus
A-27—1208	2 yrs. 8 mos.	M	104.0	.....	++++	1 day	35.0	Mastoiditis; septicemia
A-22— 648	2 yrs. 9 mos.	F	83.0	.....	+++	1 day	14.0	Pneumonia
Hammar, nos. 999, 750, 1656, 987, 749, 1567 and 1706								
von Mettenheimer, nos. 23, 34, 6, 10 and 56								

d. Congenital Defects

Friedleben 287	15 mos.	M	....	5,480	++	6 days	1.6	Cardiac defect; bronchitis
A-17— 210	2 yrs. 2 mos.	M	86.5	.....	++++	5 days	15.0	Ectopic bladder; postoperative peritonitis

e. Miscellaneous Causes

A-27— 331	2 yrs.	F	83.0	.....	++	1 day	2.7	Hematemesis; cirrhosis of liver; splenitis
Hammar, no. 890								

C. Ill One Week or More——a. Accidents

Hammar, nos. 1011, 1555 and 1021

b. Undetermined Causes

A-18— 138	16 mos.	M	81.0	10,530	+++	2 wks.	18.0	Fatty degeneration of liver and kidneys

c. Infections

A-26— 22	1 yr.	M	81.0	.....	++	3 wks.	9.0	Pneumonia; mesenteric adenitis
A-26— 716	1 yr.	M	75.5	.....	+	2 mos.	4.0	Diphtheria; myocarditis
A-17— 167	1 yr.	F	71.0	.....	+++	3 wks.	21.0	Pneumonia
A-23— 223	1 yr.	M	62.0	.....	+++	6 wks.	7.5	Pertussis; pneumonia
A-23— 292	1 yr.	M	71.0	.....	+++	3 wks.	4.0	Measles; pneumonia
A-23— 308	1 yr.	M	81.0	.....	+++	2 wks.	10.0	Bilateral pyelonephritis
Friedleben 281	1 yr. 15 days	F	....	6,306	++	10 mos.	9.1	Bronchiectasis
A-15— 303	13 mos.	M	....	.....	+	Life	17.3	Chronic bronchitis; malnutrition
A-24— 467	13 mos.	F	74.0	11,780	+++	2 wks.	9.5	Measles; pneumonia
Friedleben 284	1 yr. 2 mos.	F	....	4,560	+	Many mos.	1.3	Chronic infection of chest; pneumonia
A-19— 104	15 mos.	M	61.0	.....	+	1 mo.	30.0	Acute pericarditis
A-23— 162	15 mos.	M	68.0	.....	+	1 mo.	4.0	Miliary tuberculosis
A-27— 198	15 mos.	M	73.0	.....	+	Life	5.0	Eczema; pneumonia
A-27— 740	15 mos.	F	76.0	9,089	+++	2 wks.	4.1	Peritonitis; pneumonia
Friedleben 286	1 yr. 3 mos.	M	....	8,535	+++	13 days	6.5	Meningitis
A-28— 49	16 mos.	F	....	.....	++	5 wks.	10.0	Empyema
A-24— 431	16 mos.	M	....	11,325	+++	10 days	10.0	Scarlet fever; peritonitis; pleurisy
A-27— 215	16 mos.	F	80.0	.....	+++	3 wks.	5.5	Meningitis

TABLE 1.—*Thymus Weights Arranged According to Age, Duration of Illness and Cause of Death—Continued*

Spurce and Number	Age	Sex	Height of Body, Cm.	Weight of Body, Gm.	Nutritional Rank	Duration of Illness	Weight of Thymus, Gm.	Cause of Death
3. 1 to 3 Years—C. Ill One Week or More—c. Infections—Continued								
Friedleben 288	1 yr. 4 mos.	F	....	8,784	+++	4 wks.	12.4	Pneumonia
A-20— 107	18 mos.	M	82.0	.....	+	1 mo.	2.0	Pneumonia; ulcerative colitis
A-25— 594	18 mos.	F	82.0	.....	++	17 days	5.5	Pneumonia; ileocolitis
Friedleben 290	1 yr. 6 mos.	F	....	8,659	+++	3 wks.	5.3	Measles; pneumonia
Friedleben 291	1 yr. 6 mos.	M	....	6,840	+	Many mos.	4.3	Tuberculosis universalis
Friedleben 292	1 yr. 7 mos.	F	....	7,030	++	Many mos.	2.4	Tuberculosis universalis
Friedleben 293	1 yr. 7 mos.	M	....	7,790	++	Many wks.	3.8	Tuberculous meningitis
A-26— 600	21 mos.	F	85.0	.....	+	23 days	3.0	Acute endocarditis; streptococcus
A-18— 43	2 yrs.	M	63.5	.....	+	1 mo.	5.0	Diphtheria
A-24— 179	2 yrs.	M	73.8	.....	+	3 wks.	9.0	Unresolved pneumonia
A-25— 913	2 yrs.	M	83.0	.....	+	Life	8.0	Pneumonia
A-27—1157	2 yrs.	F	86.0	.....	+	23 days	4.0	Pneumonia; enterocolitis
A-28—1162	2 yrs.	M	104.0	.....	++	9 days	8.0	Ulcerative colitis
A-22— 163	2 yrs.	F	88.0	.....	+++	8 days	5.0	Scarlet fever
Friedleben 298	2 yrs. 1 mo.	F	....	8,652	+++	Many wks.; 12 hrs.	4.8	Pertussis
A-28— 730	2½ yrs.	F	87.0	.....	++	1 mo.	6.0	Otitis media; pneumonia
A-18— 266	2½ yrs.	F	92.0	.....	+++	10 days	10.0	Otitis media; meningitis
Friedleben 300	2½ yrs.	M	....	8,068	+	18 days	7.0	Arachnitis granulosa; hydrocephalus
Friedleben 303	2 yrs. 7 mos.	M	....	8,681	++	11 days	3.7	Tuberculous meningitis
Friedleben 304	2 yrs. 9½ mos.	F	....	6,460	++	14 days	1.6	Pertussis; pneumonia
Hammar, nos. 1332, 1682, 1338, 1452, 1276, 1634, 1027, 859, 854, 1565, 872 and 1028								
von Mettenheimer, nos. 5, 39 and 36								
d. Congenital Defects								
Hammar, nos. 1818, 942 and 1239								
e. Miscellaneous Causes								
Friedleben 285	1 yr. 2 mos.	M	....	8,097	+++	Many wks.	7.2	Rickets; pneumonia
Friedleben 283	1 yr. 2 mos.	F	....	4,180	+	Many mos.	2.1	Rickets; pneumonia
A-25— 261	15 mos.	M	76.0	.....	++++	3 wks.	15.0	Acute dilatation of heart
Friedleben 289	17 mos.	F	....	6,752	++	Many mos.	1.7	Laryngismus; severe diarrhea
A-29—1116	18 mos.	F	77.0	.....	+	Life	1.5	Chronic intestinal indigestion
Friedleben 296	1 yr. 8 mos.	F	....	5,159	+	Many mos.†	1.6	Rickets; pneumonia
Friedleben 297	1 yr. 10 mos.	F	....	7,607	++	Many mos.	4.4	Rickets; chronic bronchitis
A-27— 391	2 yrs.	F	85.0	.....	+++	3 wks.	14.6	Glioma of brain
A-27—1013	2½ yrs.	F	85.0	.....	+++	5 wks.	20.0	Purpura hemorrhagica
Hammar, nos. 958, 1317, 1795, 978 and 1387								
von Metterheimer, no. 2								
4. 3 to 5 Years—A. Ill Less Than Twenty-Four Hours—a. Accidents								
A-19— 227	3 yrs.	F	96.0	.....	+++	Found dead	28.0	Illuminating gas poisoning; incipient tuberculosis
A-25— 520	3 yrs.	M	95.0	.....	+++	1 hr.†	30.0	Strychnine poisoning
A-27— 968	3 yrs.	M	111.0	.....	+++	9 hrs.	36.0	Fracture of skull; ruptured spleen; automobile
A-29— 886	3 yrs.	M	88.0	.....	+++	16 hrs.	40.0	Fracture of skull; automobile
A-23— 243	4 yrs.	M	107.5	.....	+++	9 hrs.	47.0	Multiple fractures; internal hemorrhage; automobile

A-29— 886	3 yrs.	M	88.0	.....	+++	16 hrs.	40.0	Fracture of skull; automobile
A-23— 243	4 yrs.	M	107.5	.....	+++	9 hrs.	47.0	Multiple fractures; internal hemorrhage; automobile
A-26— 139	4 yrs.	F	99.0	.....	+++	Sudden death	30.0	Electrocution
A-27— 434	4 yrs.	M	141.0	.....	+++	20 mins.	22.0	Rupture of liver; automobile
A-29—1043	4 yrs.	F	114.0	.....	+++	6 hrs.	30.0	Fracture of skull; automobile
Hammar, nos. 1492, 1801, 1571, 1094, 1617, 1738, 757, 956 and 1799								
von Mettenheimer, nos. 9 and 28								
b. Undetermined Causes								
A-29— 78	3 yrs.	F	96.0	.....	+++	Sudden death	40.0	Convulsions
c. Infections								
A-15— 348	3½ yrs.	M	98.0	.....	+++	40 mins.	36.0	Pneumonia
Hammar, nos. 638 and 858								
d. Congenital Defects								
A-27— 99	4½ yrs.	M	109.0	.....	+++	Sudden death	39.0	Cleft palate; postoperative bronchitis
B. Ill from One to Seven Days—a. Accidents								
A-23— 606	3 yrs.	F	91.0	.....	+++	4 days	20.0	Scalding
A-28— 865	4 yrs.	M	112.0	.....	+++	2 days	30.0	Fracture of skull; meningitis; automobile
A-26—1094	4 yrs.	M	110.0	.....	+++	3 days	19.0	Rupture of bladder; automobile
b. Undetermined Causes								
A-21— 31	4 yrs.	M	93.0	.....	+++	1 day	32.0	Diarrhea
A-25— 764	4 yrs.	F	102.0	.....	+++	1 day	22.0	Fever
c. Infections								
A-28—1622	3 yrs.	M	92.0	.....	+++	3 days	20.0	Diphtheria; pneumonia
A-27— 304	3 yrs.	F	90.0	.....	++	2 days	7.0	Meningitis; meningococcus
A-18— 141	3 yrs.	M	99.5	.....	+++	4 days	20.0	Diphtheria
A-25— 590	3½ yrs.	M	100.0	.....	+++	2 days	20.0	Poliomyelitis
A-25— 882	4 yrs.	M	103.5	.....	+++	3 days	20.0	Suppurative pericarditis and pleuritis
A-26— 407	4 yrs.	M	....	.....	++	2 days	20.0	Diphtheria
A-23— 158	4 yrs.	F	....	.....	+++	1 day	15.0	Enterocolitis
Hammar, nos. 856, 1223, 784 and 789								
C. Ill One Week or More—a. Accidents								
A-17— 158	4 yrs.	M	99.0	.....	+++	1 wk.	31.0	Multiple hemorrhages into spinal cord from fall
A-25— 992	4 yrs.	F	110.0	.....	+++	2 wks.	22.3	Tracheitis one day after removal of foreign body from bronchus
Hammar, no. 801								
c. Infections								
A-16— 315	3 yrs.	M	96.0	.....	+++	11 days	30.0	Poliomyelitis
A-17— 168	3 yrs.	M	92.0	.....	+++	2 wks.	19.0	Pneumonia
A-25— 974	3 yrs.	F	98.0	.....	+++	7 wks.	8.5	Rheumatic endocarditis and pericarditis
A-27— 553	3 yrs.	M	93.0	.....	+++	2 wks.	14.1	Pneumonia; meningitis
A-28— 420	3 yrs.	M	94.0	.....	+++	5 wks.	12.0	Mastoiditis; meningitis
Friedleben 305	3 yrs. 5 mos.	M	....	8,046	+	1½ yrs.	2.4	Pulmonary and intestinal tuberculosis
A-24— 419	3½ yrs.	M	93.5	.....	+	Few weeks†	4.0	Scarlet fever; adenitis; pneumonia
A-27— 480	3½ yrs.	M	105.0	.....	+	4 mos.	5.8	Meningitis; streptococcus
Friedleben 306	3 yrs. 7 mos.	F	....	12,686	+	19 days	4.5	Typhus abdominalis
Friedleben 307	3 yrs. 9 mos.	F	....	11,736	++	13 days	6.1	Croup; tracheotomy

TABLE 1.—*Thymus Weights Arranged According to Age, Duration of Illness and Cause of Death—Continued*

Source and Number	Age	Sex	Height of Body, Cm.	Weight of Body, Gm.	Nutritional Rank	Duration of Illness	Weight of Thymus, Gm.	Cause of Death
4. 3 to 5 Years—C. Ill One Week or More——c. Infections—Continued								
A-25— 142	4 yrs.	F	143.0	.....	+++	1 mo.	14.0	Malignant endocarditis
A-26— 720	4 yrs.	M	....	.....	+++	2 wks.	14.0	Diphtheria; myocarditis
A-25— 563	4 yrs.	M	100.0	.....	+	3 wks.	4.0	Tuberculosis
A-25— 641	4 yrs.	M	107.0	.....	+	3 wks.	3.5	Tuberculosis
A-26— 405	4 yrs.	F	104.0	.....	++	2 wks.	8.0	Measles; pneumonia
A-26— 864	4 yrs.	F	103.0	.....	++	2 wks.	5.0	Measles; pneumonia
Friedleben 308	4 yrs.	F	....	10,377	+	14 days	7.5	Typhus abdominalis
Friedleben 309	4 yrs. 5 mos.	F	....	10,274	+	7 wks.	3.1	Pertussis; pneumonia
Friedleben 310	4 yrs. 6 mos.	M	....	14,308	+	14 days	5.1	Tuberculosis
Friedleben 311	4 yrs. 9 mos.	M	....	10,785	+	Few mos.† 10 days	1.2	Tuberculous meningitis
Hammar, nos. 1312, 1150, 1697, 1014, 938, 1648, 1034, 860, 862, 1340, 1624, 1134, 1367, 1235 and 1139								
von Mettenheimer, nos. 21, 3, 11 and 29								
d. Congenital Defects								
A-12— 118	4 yrs. 5 mos.	M	60.0	.....	+++	4 yrs.†	15.0	Meningomyelocele
e. Miscellaneous Causes								
Hammar, nos. 1421 and 1019								
f. Exophthalmic Goiter and Leukemia								
A-26—1030	3½ yrs.	F	103.0	.....	++	4 mos.	4.0	Acute lymphatic leukemia
5. 5 to 10 Years——A. Ill Less Than Twenty-Four Hours——a. Accidents								
A-24— 404	5 yrs.	F	109.0	.....	+++	Found dead	40.0	Fracture of skull; automobile
A-25—1013	5 yrs.	M	96.0	.....	+++	15 mins.	50.0	Strychnine poisoning
A-26— 345	5 yrs.	F	110.0	.....	++++	30 mins.	38.0	Rupture of liver and lungs; automobile
A-26— 385	5 yrs.	M	101.5	.....	+++	3 hrs.	17.0	Fracture of skull; rupture of liver; automobile
A-27— 996	5 yrs.	M	106.0	.....	+++	5 hrs.	25.0	Cerebral hemorrhage; automobile
A-28— 782	5 yrs.	F	110.0	.....	+++	Few mins.†	42.5	Fracture of skull; automobile
A-28—1400	5 yrs.	M	118.0	.....	+++	Few mins.†	35.0	Fracture of skull; automobile
A-29— 17	5 yrs.	F	108.0	.....	+++	Few mins.†	35.0	Subdural hemorrhage; train
A-11— 36	5 yrs. 10 mos.	M	107.0	.....	+++	18 hrs.	20.0	Fish poisoning
A-16— 314	6 yrs.	F	92.0	.....	+++	12 hrs.	28.0	Illuminating gas poisoning
A-23— 199	6 yrs.	M	115.0	.....	+++	Few mins.†	32.0	Internal hemorrhage
A-25— 879	6 yrs.	M	....	.....	+++	12 hrs.	15.0	Hemoperitoneum; leg cut off by train
A-26— 411	6 yrs.	F	120.0	.....	+++	Sudden death	25.0	Fracture of spine; automobile
A-26— 587	6 yrs.	F	116.0	.....	+++	Found dead	30.0	Chloroform poisoning
A-27— 687	6 yrs.	M	116.0	.....	+++	20 hrs.	22.0	Cerebral hemorrhage; automobile
A-28— 399	6 yrs.	M	117.0	.....	+++	Few mins.†	25.0	Fracture of skull; rupture of aorta; automobile
A-29— 890	6 yrs.	M	111.0	.....	+++	2 hrs.	55.0	Rupture of vena cava; automobile
A-29—1576	6 yrs.	F	112.0	.....	+++	17 hrs.	30.0	Fracture of skull; street car
	6 yrs.	F	114.0	.....	++	Few mins.†	23.0	Rupture of liver; automobile

A-29— 890	6 yrs.	M	111.0	.....	+++	2 hrs.	55.0	Rupture of vena cava; automobile
A-29—1576	6 yrs.	F	112.0	.....	+++	17 hrs.	30.0	Fracture of skull; street car
A-27—1242	8 yrs.	F	114.0	.....	++	Few mins.†	23.0	Rupture of liver; automobile
A-29— 846	8 yrs.	F	137.0	.....	+++	2 hrs.	50.0	Rupture of liver; automobile
A-23— 311	9 yrs.	F	....	.....	+++	2 hrs.	40.0	Rupture of liver; automobile
A-24— 376	9 yrs.	M	....	.....	+++	3 hrs.	27.4	Fracture of pelvis; automobile
A-20— 439	9 yrs.	M	127.0	.....	++	Few mins.†	28.6	Fracture of skull; automobile
Hammar, nos. 1429, 1776, 1583, 1803, 814, 1417, 699:6, 1615, 1748, 1806, 1758, 1616, 1085, 1859, 1661, 1804, 1414, 1689, 1742, 1427, 1802, 1585, 1614, 1729, 982, 1655, 1654, 1712 and 1690								
				b. Undetermined Causes				
A-29—1842	5 yrs.	M	113.0	.....	+++	12 hrs.	30.0	Respiration difficult
A-21— 125	5½ yrs.	M	118.0	.....	++	12 hrs.	46.0	Cloudy swelling of viscera
Hammar, no. 776								
				c. Infections				
Hammar, nos. 1201, 755 and 639								
				B. Ill from One to Seven Days——a. Accidents				
A-28— 877	5 yrs.	F	109.0	.....	+++	1 day	8.0	Multiple fractures; automobile
A-26— 589	5 yrs.	M	103.0	.....	+++	1 day	33.0	Cerebral hemorrhage; automobile
A-27— 111	6½ yrs.	F	113.0	.....	+++	3 days	17.0	Fracture of skull; automobile
A-26— 767	7 yrs.	M	126.0	.....	+++	1 day	20.0	Ruptured ileum; fell from truck
A-29— 829	8 yrs.	M	126.0	.....	+++	1 day	35.0	Ruptured liver and spleen; automobile
A-28— 721	8 yrs.	M	124.0	.....	++	1 day	50.0	Fracture of skull and pelvis; automobile
Hammar, nos. 1464, 1855 and 1700								
				b. Undetermined Causes				
A-23— 253	5 yrs.	M	85.0	.....	+++	3 days	28.5	Infectious course clinically
A-28— 290	6 yrs.	M	107.8	.....	++	1 day	17.0	Pneumonia ?; temperature 103 F.
				c. Infections				
Friedleben 314	5 yrs. 8 mos.	F	.....	13,227	+++	6 days	7.7	Laryngotracheobronchitis exudativa
A-24— 544	6 yrs.	M	111.0	.....	++	5 days	20.0	Pneumonia; meningitis
A-22— 349	6 yrs.	M	119.0	.....	+++	1 day	30.0	Tetanus
A-27— 812	7 yrs.	M	120.0	.....	++	5 days	20.0	Meningitis
Hammar, nos. 875, 865, 751, 748, 1815, 1063, 1769, 1700, 752, 972, 1453, 1761, 1270, 1703 and 1358								
von Mettenheimer, nos. 24, 18, 37, 27 and 53								
				C. Ill One Week or More——a. Accidents				
A-27— 61	7 yrs.	M	116.0	.....	++	4 mos.	11.5	Pericarditis and pleuritis after rupture of diaphragm; automobile
Hammar, no. 794								
				b. Undetermined Causes				
A-28— 594	7 yrs.	F	114.0	.....	+++	3 wks.	20.0	Infectious course clinically
				c. Infections				
A-26— 388	5 yrs.	M	102.0	.....	+++	10 days	9.6	Diphtheria
A-15— 189	5 yrs.	M	109.0	.....	++	20 days	16.0	Rabies
A-16— 86	5 yrs.	F	108.0	.....	+	3 wks.	3.0	Polyserositis; streptococcus
A-24— 264	5 yrs.	F	100.0	.....	++	2 wks.	15.0	Pneumonia
Friedleben 312	5 yrs.	M	.....	10,845	+	14 days	1.5	Measles; gangrene of lung

TABLE 1.—*Thymus Weights Arranged According to Age, Duration of Illness and Cause of Death—Continued*

Source and Number	Age	Sex	Height of Body, Cm.	Weight of Body, Gm.	Nutritional Rank	Duration of Illness	Weight of Thymus, Gm.	Cause of Death
5. 5 to 10 Years——C. Ill One Week or More——c. Infections—Continued								
Friedleben 313	5 yrs.	F	.....	11,429	++	14 days	3.4	Suppurative meningitis
A-26— 372	6 yrs.	M	89.0	.....	+	1 mo.	8.5	Peritonitis; pneumonia
A-26— 468	6 yrs.	F	119.0	.....	++	14 days	8.0	Scarlet fever; meningitis
A-27— 963	6 yrs.	M	113.0	.....	+	22 days	4.0	Enterocolitis
A-10— 5	6 yrs.	F	116.0	.....	+	2 mos.	25.0	Poliomyelitis; pneumonia
A-15— 235	6 yrs. 10 mos.	F	120.0	.....	+++	13 days	15.0	Vincent's angina
A-26— 844	7 yrs.	M	124.0	.....	++	14 mos.	13.0	Purpura; pneumonia
A-29— 365	7 yrs.	M	101.7	.....	++	5½ yrs.	30.0	Tuberculosis of spine; postoperative shock
A-25— 798	8 yrs.	F	127.0	.....	++	8 wks.	15.0	Scarlet fever; nephritis
A-28—1181	8½ yrs.	F	121.0	.....	+	1 yr.	31.0	Chronic osteomyelitis; postoperative shock
Friedleben 317	8 yrs. 7 mos.	M	.....	19,409	+++	3 wks.	8.5	Pericarditis; endocarditis
A-25— 689	9 yrs.	F	143.9	.....	++	3 wks.	9.0	Mastoiditis; meningitis
A-27—1183	9 yrs.	M	131.0	.....	+	12 days	5.0	Diphtheria
Hammar, nos. 914, 1357, 1426, 866, 1337, 1437, 1018, 1401, 1204, 1705, 1759, 871, 1066, 1637, 1764, 1498, 1321, 1304, 1035 and 1218								
von Mettenheimer, no. 13								
e. Miscellaneous Causes								
A-16— 34	5 yrs.	F	96.0	.....	++	3 mos.	6.0	Sarcoma of brain
A-22— 12	6 yrs.	M	117.0	.....	+	1 mo.	8.0	Purpura hemorrhagica
A-26— 828	6 yrs.	M	111.0	.....	+	3 mos.	9.0	Brain tumor
A-21— 543	6 yrs.	F	.....	.....	+++	Few wks.	10.0	Brain tumor; postoperative pneumonia
Friedleben 315	6 yrs.	M	.....	12,854	+	7 mos.	0.9	Steatoma of suprarenal
A-18— 50	9 yrs.	M	120.0	.....	+	1 yr.	20.0	Cerebellar tumor
Hammar, nos. 931, 1677, 1447, 1642, 1422, 1816 and 1831								
f. Exophthalmic Goiter and Leukemia								
A-25— 540	6 yrs.	M	113.0	.....	+	4 mos.	5.0	Lymphatic leukemia
6. 10 to 15 Years——A. Ill Less Than Twenty-Four Hours——a. Accidents								
A-20— 236	10 yrs.	M	.....	.....	+++	30 mins.	30.0	Rupture of liver; automobile
A-26— 575	10 yrs.	F	135.0	.....	+++	Few mins.†	25.0	Fracture of skull; automobile
A-27— 636	10 yrs.	M	144.0	.....	+++	½ hr.	35.0	Fracture of skull; rupture of liver; automobile
A-27— 939	10 yrs.	F	138.0	.....	+++	Few mins.†	14.0	Rupture of liver; fell out of window
A-15— 227	11 yrs.	F	137.0	.....	+++	3 hrs.	33.0	Rupture of liver; automobile
A-26—1119	11 yrs.	M	138.0	.....	++	25 mins.	36.5	Fracture of spine; rupture of viscera; automobile
A-28— 825	12 yrs.	M	137.0	.....	++	3 hrs.	50.0	Fracture of skull; automobile
A-29—1864	12 yrs.	F	151.0	.....	++	Few mins.†	35.0	Fracture of skull; automobile
A-17— 131	13 yrs.	M	139.0	.....	++	Found dead	27.8	Shot in chest
A-22— 628	13 yrs.	M	148.0	.....	++	Few hrs.†	25.0	Fracture of skull; automobile
A-20— 31	13 yrs.	M	147.0	.....	+++	Found dying	22.0	Illuminating gas poisoning
						1 hr.	50.0	Rupture of liver, spleen and kidney

A-20— 31	13 yrs.	M	147.0	.....	+++	Found dying	22.0	Illuminating gas poisoning
A-25— 656	13 yrs.	M	143.0	.....	+++	1 hr.	50.0	Rupture of liver, spleen and kidney
A-27— 782	13 yrs.	M	150.0	.....	+++	7 hrs.	40.0	Fracture of skull; automobile
Hammar, nos. 1086, 1749, 1582, 1849, 1691, 1713, 1807, 1693, 1066, 1572, 1670, 697, 1438, 1791, 1065, 1757, 1756, 1687, 967, 1686, 1739, 1692, 1696, 1688, 1454 and 1613								
Dustin and Zunz, no. 38								
				b. Undetermined Causes				
A-26— 887	12 yrs.	F	156.0	.....	+++	11 hrs.	35.0	Nitrous oxide and ether anesthesia for operation on injured finger
A-21— 266	14 yrs.	M	159.0	.....	+++	Sudden death	45.0	Ether anesthesia for operation on chronic mastoiditis
Hammar, nos. 1854 and 1006								
				d. Congenital Defects				
Hammar, no. 1490								
				e. Miscellaneous Causes				
Hammar, no. 1073								
				B. Ill from One to Seven Days——a. Accidents				
A-29— 605	12 yrs.	M	144.0	.....	+++	2 days	16.0	Fracture of skull; hit by stone
A-26— 507	13 yrs.	M	150.0	.....	+++	2 days	45.0	Fracture of skull; automobile
Hammar, nos. 793, 802, 1148 and 1612								
				e. Infections				
A-21— 331	10 yrs.	M	142.0	.....	+++	3 days	35.0	Pneumonia
A-23— 571	10 yrs.	M	136.0	.....	+++	6 days	18.0	Meningitis
A-22— 107	10 yrs.	M	141.0	.....	++	6 days	15.0	Appendicitis; peritonitis
A-28—1239	10 yrs.	M	142.0	.....	++	5 days	20.0	Poliomyelitis
Friedleben 319	10 yrs. 8 mos.	M	.....	21,455	+++	40 hrs.	19.9	Scarlet fever
A-16— 297	11 yrs.	M	145.0	.....	+++	4 days	35.0	Poliomyelitis
A-27— 971	11 yrs.	M	139.0	.....	++	4 days	5.0	Pneumonia; tetanus
A-11— 20	14 yrs.	F	155.0	.....	+++	3 days	10.0	Peritonitis
A-22— 399	14 yrs.	M	165.0	.....	++	6 days	5.0	Meningitis
Hammar, nos. 988, 656, 857, 745, 746 and 744								
				e. Miscellaneous Causes				
Hammar, nos. 853 and 754								
				C. Ill One Week or More——c. Infections				
A-24— 608	10 yrs.	M	156.0	.....	+	Life	15.0	Dementia paralytica
A-26— 70	10 yrs.	M	133.0	.....	+	23 days	14.0	Empyema
A-26—1014	10 yrs.	F	132.0	.....	++	2 mos.	10.0	Acute rheumatic fever; endocarditis
Friedleben 318	10 yrs. 6 mos.	F	.....	22,683	++	17 days	5.8	Typhus abdominalis
A-27— 847	12 yrs.	F	.....	.....	+++	10 days	20.0	Pyemia
A-26— 64	12 yrs.	M	138.0	.....	+++	Life	25.0	Hematemesis; syphilitic cirrhosis of liver
A-19— 209	13 yrs.	F	136.0	.....	+++	3 wks.	20.0	Tetanus
Friedleben 320	13 yrs. 4 mos.	F	.....	28,062	+	Many yrs.	9.5	Empyema; fibrosis of lungs; anasarca
Hammar, nos. 1383, 1594, 1351, 1379, 1047, 1675, 1658, 1455, 874, 1280, 1579, 921, 941, 1681, 1793, 1796, 1290, 1554, 1839, 1537, 1626 and 1568								
				d. Congenital Defects				
A-21— 536	11 yrs.	F	.....	.....	+	Life; 1 day	10.0	Cardiac defect; died following tonsillectomy

TABLE 1.—*Thymus Weights Arranged According to Age, Duration of Illness and Cause of Death—Continued*

Source and Number	Age	Sex	Height of Body, Cm.	Weight of Body, Gm.	Nutritional Rank	Duration of Illness	Weight of Thymus, Gm.	Cause of Death
6. 10 to 15 Years—C. Ill One Week or More—Continued—e. Miscellaneous Causes								
A-27— 600	13 yrs.	M	155.0	.....	++++	Few mos.†	25.0	Glioma of cerebellum
Hammar, no 1784								
von Mettenheimer, no. 43								
f. Exophthalmic Goiter and Leukemia								
A-26—1091	12 yrs.	M	148.0	.....	+++	14 days	106.0	Acute lymphatic leukemia
A-27— 218	12 yrs.	M	144.0	.....	+	2 mos.	22.5	Exophthalmic goiter
7. 15 to 20 Years—A. Ill Less Than Twenty-Four Hours—a. Accidents								
A-25—1010	15 yrs.	M	167.0	.....	+++	Few mins.†	15.0	Shot in chest
A-29— 222	15 yrs.	M	163.5	.....	++	Few mins.†	38.0	Fracture of cervical spine; automobile
A-16— 238	16 yrs.	M	169.0	.....	+++	4 hrs.	35.0	Rupture of liver; automobile
A-21— 302	18 yrs.	M	168.0	.....	+++	1 hr.	46.0	Stab wound of liver and vena cava
A-26—1013	18 yrs.	M	179.0	.....	++	5 hrs.	10.0	Fracture of skull; collision of street car and automobile
Hammar, nos. 1694, 625, 1850, 968, 694, 627, 1800, 965, 1851, 923, 1458, 960, 742, 917 and 1463								
b. Undetermined Causes								
A-29— 837	19 yrs.	M	175.0	.....	+++	Few mins.†	15.0	Blow in abdomen
c. Infections								
Hammar, no. 1056								
e. Miscellaneous Causes								
A-18— 255	16 yrs.	M	175.0	.....	+++	Found dead	36.0	Hypertension; glomerular sclerosis
A-29—1788	19 yrs.	M	183.0	.....	+++	Few mins.†	63.0	Dilatation of heart
A-23— 478	19 yrs.	F	161.0	.....	+++	Few hrs.†	40.0	Fat embolus; extension of joint
Hammar, nos. 1779 and 641								
B. Ill from One to Seven Days—a. Accidents								
Hammar, nos. 1462, 981, 1496, 916, 1521 and 1745								
Dustin and Zunz, nos. 6 and 9								
c. Infections								
A-26— 461	15 yrs.	M	157.0	.....	+++	5 days	18.0	Appendicitis; postoperative pneumonia
A-28—1143	17 yrs.	M	160.0	.....	+++	3 days	15.0	Poliomyelitis
Hammar, nos. 1364, 1300, 1645, 1650, 1020 and 902								
e. Miscellaneous Causes								
Hammar, nos. 1060 and 1590								
C. Ill One Week or More—c. Infections								
Hammar, nos. 1359, 1248, 1335, 1238, 950, 1262, 1284, 1639, 1187, 1166, 1253, 1322, 723, 855, 1512, 1267 and 1135								

d. Congenital Defects

1322, 723, 855, 1512, 1267 and 1135								

d. Congenital Defects

Hammar, no. 1597								

e. Miscellaneous Causes

A-21— 60	16 yrs.	F	157.0	.....	++++	Few yrs.†	25.0	Glioma of midbrain
Hammar, nos. 1627, 722, 1477, 1788, 1425, 1643, 983, 1053, 901, 895, 899 and 1701								

f. Exophthalmic Goiter and Leukemia

A-25— 534	16 yrs.	F	152.0	.....	+++	3 mos.	150.0	Lymphatic leukemia
A-22— 434	18 yrs.	F	159.0	.....	++	8 mos.	38.0	Exophthalmic goiter
Hammar, nos. 1586, 739, 1812 and 773								

S. 20 to 25 Years——A. Ill Less Than Twenty-Four Hours——a. Accidents

A-26—1035	20 yrs.	M	176.0	.....	+++	Few mins.†	30.0	Illuminating gas poisoning
A-25— 678	22 yrs.	M	161.0	.....	+++	2 hrs.	20.0	Multiple fractures; rupture of liver; elevator
A-17— 120	23 yrs.	F	158.0	.....	++++	Found dead	22.0	Chloroform poisoning
A-16— 402	24 yrs.	F	163.0	.....	+++	3 hrs.	15.0	Anesthesia with a proprietary coccaine mixture
Hammar, nos. 1503, 883, 650, 783, 1467, 1466, 1009, 1651, 1542, 740, 969, 1476, 1245, 1805, 891, 911, 804, 1117, 1528, 979, 1563, 1574, 1494, 1575, 920, 1412, 961 and 629								
Dustin and Zunz, nos. 18, 26, 8, 34, 35, 37, 2, 5, 10, 13, 14, 16, 20, 21, 22, 23, 28 and 30								

b. Undetermined Causes

A-22— 239	20 yrs.	M	180.0	.....	+++	Died suddenly	35.0	Serous exudate in lungs
Hammar, nos. 649 and 778								

e. Miscellaneous Causes

Hammar, no. 1297								

B. Ill from One to Seven Days——a. Accidents

Hammar, nos. 1360, 927, 803 and 1760								
Dustin and Zunz, nos. 1, 17 and 19								

c. Infections

Hammar, nos. 873, 922, 1192, 933, 915, and 464								

e. Miscellaneous Causes

A-22— 492	23 yrs.	F	168.0	.....	++	3 days	50..0	Perforation of repair of fecal fistula
Hammar, no. 1049								

C. Ill One Week or More——c. Infections

A-24— 841	20 yrs.	F	160.0	.....	++	12 days	10.0	Tuberculous meningitis; pregnancy
Hammar, nos. 1200, 1324, 1173, 1236, 1213, 1133, 1710, 1442, 1404, 1792, 1197, 1269, 1319, 1479, 1306, 1378, 1114, 1163, 1221, 1205, 1193, 1196, 1177, 1278, 1243, 1216, 1234, 1246, 1538, 1249, 1299, 1708, 1183, 1182, 1159, 1141, 1268, 1229 and 1457								

e. Miscellaneous Causes

A-16— 354	20 yrs.	M	.....	.....	+	2 mos.	10.0	Sarcoma of cerebellum
Hammar, nos. 1659, 1475, 1398, 759, 1825 and 1348								

TABLE 1.—*Thymus Weights Arranged According to Age, Duration of Illness and Cause of Death—Continued*

Source and Number	Age	Sex	Height of Body, Cm.	Weight of Body, Gm.	Nutritional Rank	Duration of Illness	Weight of Thymus, Gm.	Cause of Death
8. 20 to 25 Years—C. Ill One Week or More—Continued—f. Exophthalmic Goiter and Leukemia								
A-22— 487	24 yrs.	F	162.0	.....	+++	8 yrs.	45.0	Exophthalmic goiter; died following operation
A-24— 55	24 yrs.	F	159.0	.....	+	3 yrs.	45.0	Exophthalmic goiter
Hammar, nos. 767, 1393 and 771								
9. 25 to 30 Years—A. Ill Less Than Twenty-Four Hours—a. Accidents								
A-15— 336	25 yrs.	M	148.0	.....	+++	2½ hrs.	11.0	Shot in abdomen
A-24— 402	26 yrs.	M	179.0	.....	+++	Few hrs.†	40.0	Epilepsy; cerebral hemorrhage; fell downstairs
Hammar, nos. 643, 1194, 1313, 926, 647, 1843, 743, 881, 699, 1724, 937, 805, 1459, 1354, 1499, 1527, 1483, 1777, 1468, 1622 and 959								
Dustin and Zunz, nos. 6, 12, 32, 15, 27, 29 and 31								
b. Undetermined Causes								
A-16— 269	25 yrs.	M	166.0	.....	+++	Found dead	25.0	Acute poisoning; alcoholism ?
Hammar, nos. 935 and 756								
c. Infections								
Hammar, no. 1415								
e. Miscellaneous Causes								
Hammar, no. 1052								
B. Ill from One to Seven Days—a. Accidents								
Dustin and Zunz, no. 33								
c. Infections								
Hammar, nos. 747, 1198 and 1167								
e. Miscellaneous Causes								
Hammar, nos. 1136 and 1279								
C. Ill One Week or More—c. Infections								
A-17— 28	29 yrs.	M	166.0	.....	+++	11 mos.	5.0	Chronic and acute endocarditis; peritonitis
A-23— 521	29 yrs.	F	168.0	.....	++++	8 days	40.0	Laryngeal diphtheria
Hammar, nos. 1222, 1264, 1120, 1318, 1350, 1171, 1625, 1252, 1232, 1384, 1190, 1185, 1228, 1308, 1217, 1265, 1162, 1224, 1121, 1266, 1145, 1147, 1170, 1225, 1151, and 1172								
e. Miscellaneous Causes								
A-26— 295	25 yrs.	F	167.0	.....	++	1 mo.	20.0	Postpartum psychosis
Hammar, nos. 1153, 1023, 1303, 1428, 1144, 1315, 1536 and 1833								
f. Exophthalmic Goiter and Leukemia								
Hammar, nos. 726, 737, 1813, 730, 1778, 725, 765, 769, 1386 and 1540								
10. 30 to 40 Years—A. Ill Less Than Twenty-Four Hours—a. Accidents								
A-15— 328	30 yrs.	M	183.0	.....	+++	Found dead	22.0	Rupture of liver; found in railroad yards
A-27— 409	31 yrs.	M	169.5	.....	+++	Found dead	25.0	Acute alcoholism
A-22— 408	32 yrs.	M	175.0	.....	++	1 day†	30.0	Heat shock
A-19— 129	32 yrs.	M	168.0	.....	+++	2½ hrs.	30.0	Fracture of skull; automobile
A-19— 127	33 yrs.	M	174.0	.....	+++	1 hr.	30.0	Shot in abdomen and chest

A-22— 408	32 yrs.	M	175.0	.....	++	1 day†	30.0	Heat shock
A-19— 129	32 yrs.	M	168.0	.....	+++	2½ hrs.	30.0	Fracture of skull; automobile
A-19— 127	33 yrs.	M	174.0	.....	+++	1 hr.	30.0	Shot in abdomen and chest
A-23— 481	34 yrs.	M	179.0	.....	+++	3 hrs.	30.0	Fracture of cervical spine; wrestling
A-24— 491	38 yrs.	M	181.0	.....	+++	5 hrs.	37.0	Blow on head; cerebral hemorrhage; old tuberculosis
Hammar, nos. 1674, 1508, 699:9, 806, 1440, 1746, 1091, 807, 1400, 880, 1061, 852, 898, 631, 909, 980, 651, 632, 1504, 1058, 684, 919, 1074, 1301, 1472, 1062, 1461, 1546 and 1578								
Dustin and Zunz, nos. 24, 4, 25 and 36								
				c. Infections				
A-27— 190	37 yrs.	M	173.0	.....	+++	Found dead	26.0	Influenza; pneumonia; streptococcus
				e. Miscellaneous Causes				
A-26— 957	34 yrs.	M	172.0	.....	+++	Sudden death	38.0	Cerebral hemorrhage
Hammar, nos. 1577 and 1063								
				B. Ill from One to Seven Days——a. Accidents				
Hammar, nos. 885, 1664, 1502 and 878								
				c. Infections				
A-15— 184	35 yrs.	M	160.0	.....	+++	4 days	25.0	Pneumonia
Hammar, nos. 1059, 1785, 791, 1762, 1025 and 1226								
				e. Miscellaneous Causes				
Hammar, no. 1846								
				C. Ill One Week or More——c. Infections				
Hammar, nos. 1596, 1188, 1064, 1287, 1647, 1621, 1247, 1672, 1560, 1419, 1174, 1231, 1203, 1255, 1250, 1599, 1837, 1644, 1296, 1277, 1311, 1744, 1242, 1282, 1580, 1257, 1251, 1230, 1007, 1283, 1195, 1233, 1446, 1050, 1763, 1365, 1289, 1631 and 1316								
				e. Miscellaneous Causes				
A-28— 669	33 yrs.	M	169.0	.....	+	Few yrs.†	16.6	Myasthenia gravis; pneumonia
Hammar, nos. 1362, 1448, 1525, 1630, 1535, 1765, 1471, 1794, 1819, 1488, 1368 and 932								
				f. Exophthalmic Goiter and Leukemia				
A-25— 566	30 yrs.	F	165.0	.....	++	1 yr.	45.0	Exophthalmic goiter; pneumonia
A-23— 129	32 yrs.	F	162.0	.....	++	1 yr.	21.0	Exophthalmic goiter
Hammar, nos. 729, 992, 1119, 734, 764, 763, 770, 1003, 727, 1045, 1753, 1857, 731, 1828, 733, 735, 1714 and 1726								
				11. 40 to 60 Years——A. Ill Less Than Twenty-Four Hours——a. Accidents				
A-26— 665	42 yrs.	F	150.0	.....	+	Found dead	25.0	Drowning
A-26—1114	43 yrs.	M	155.0	.....	+++	Few mins.†	44.0	Fracture of skull; automobile
Hammar, nos. 1372 633, 1063, 1526, 1752, 1068, 1541, 1273, 1522, 1399, 1481, 699:10, 682, 1054, 648, 1484, 1493 1482, 695 and 1010								
				b. Undetermined Causes				
Hammar, no. 1413								
				e. Miscellaneous Causes				
Hammar, nos. 1004, 1840, 1500, 1649, 1501 and 1619								
				B. Ill from One to Seven Days——a. Accidents				
Hammar, nos. 924 and 720								
				c. Infections				
A-28— 101	54 yrs.	M	176.0	.....	+++	6 days	45.0	Otitis media; mastoiditis; pneumonia
Hammar, nos. 792, 1385 and 1184								

TABLE 1.—*Thymus Weights Arranged According to Age, Duration of Illness and Cause of Death—Continued*

Source and Number	Age	Sex	Height of Body, Cm.	Weight of Body, Gm.	Nutritional Rank	Duration of Illness	Weight of Thymus, Gm.	Cause of Death
	11. 40 to 60 Years——B. Ill from One to Seven Days—Continued——e. Miscellaneous Causes							
Hammar, no. 1860								
	C. Ill One Week or More—b. Undetermined Causes							
Hammar, no, 1161								
	c. Infections							
Hammar, nos. 1296, 1057, 1180, 1219, 1388, 1699, 1519, 1051, 879, 1220, 1292, 1636, 1142, 1356, 1275, 1254, 1075, 1770, 1518, 1189, 1344, 1588, 1302, 1766, 1111, 1149, 1143 and 1495								
	e. Miscellaneous Causes							
A-12— 128	40 yrs.	M	180.0	.....	+	Few mos.†	17.5	Brain tumor
A-28—1310	50 yrs.	F	162.5	.....	+	14 yrs.	16.0	Addison's disease
A-28—1373	54 yrs.	M	172.0	.....	+	5 yrs.	18.0	Myasthenia gravis; pneumonia
A-22— 231	59 yrs.	F	165.0	.....	+	2 yrs.	35.0	Acute combined sclerosis
Hammar, nos. 1436, 1515, 1032, 912, 984, 1553, 1395, 1783, 1652, 1741, 1497, 1291, 1564, 1834, 1750, 1256, 1832, 1513, 1581, 782, 1600, 1043, 1309, 1598, 1307, 1727, 1858, 1186, 1155, 762, 1179, 1175, 1293, 1629, 1168, 1241 and 925								
	† Exophthalmic Goiter and Leukemia							
A-19— 36	40 yrs.	M	182.0	.....	+	4 yrs.	60.0	Exophthalmic goiter
Hammar, nos. 772, 766, 774, 732, 728, 1491, 760, 768, 1013, 1653, 761, 775 and 1341								
	12. 60 to 90 Years—A. Ill Less Than Twenty-Four Hours——a. Accidents							
Hammar, nos. 1001, 646, 642, 1373, 1573, 652, 1523, 1725, 1842, 1003, 636, 696, 1558, 788, 884, 1514, 1072 and 637								
	e. Miscellaneous Causes							
Hammar, nos. 1623 and 1140								
	B. Ill from One to Seven Days——c. Infections							
Hammar, nos. 1288 and 1402								
	e. Miscellaneous Causes							
Hammar, no. 1620								
	C. Ill One Week or More——a. Accidents							
Hammar, nos. 1240 and 1663								
	e. Infections							
Hammar, nos. 736, 1396, 1271, 1258, 1227, 1361 and 1122								
	e. Miscellaneous Causes							
A-16— 366	60 yrs.	F	164.0	.....	+	6 mos.	1.0	Asphyxia from colloid goiter
A-27— 743	64 yrs.	F	156.0	.....	++	Few yrs.†	60.0	Cancer of lung; adenomatous goiter
Hammar, nos. 1115, 1366, 900, 1635, 1768, 1202, 1403, 1394, 1374, 1389, 1678, 1214, 1272, 1545, 1285, 1263, 1339, 1326, 1181, 1154, 1116, 1628, 1156, 1370, 1157, 1303, 1369 and 1164								
	f. Exophthalmic Goiter and Leukemia							
Hammar, nos. 1633, 1829 and 1552								

of normal thymuses weigh less than the median weight, while 50 per cent weigh more; 25 per cent weigh less than the weight at the 25 percentile, while 75 per cent weigh more, and so on for the 75, 10

TABLE 2.—*Median Weight and Range in Weight of the Normal Thymus Gland* *

Age Interval	No. Cases	Median Age	Median Weight, Gm.	Range of Weight, Gm.		
				Interquartile	10 to 90 Percentile	Minimum to Maximum
Birth to 24 hr.	56	5 hr.	10.9	8.2-14.9	6.5-17.5	3.5-31.0
24 hr. to 1 yr.	11	7 wk.	19.5	10.9-27.8	5.5-29.9	4.3-31.0
1 to 3 yr.	17	2 yr.	23.0	16.9-34.0	8.5-51.0	7.0-55.0
3 to 5 yr.	19	4 yr.	28.0	20.0-31.0	16.5-38.5	13.5-47.0
5 to 10 yr.	52	6 yr.	28.5	23.5-35.0	19.0-46.0	15.0-55.0
10 to 15 yr.	40	11 yr.	29.5	24.5-36.0	19.5-42.0	13.0-50.0
15 to 20 yr.	20	17 yr.	21.0	16.5-34.5	13.5-44.0	10.0-49.7
20 to 25 yr.	50	23 yr.	18.6	13.0-25.0	9.9-30.8	7.0-51.0
25 to 30 yr.	30	26.5 yr.	16.5	11.9-23.5	8.7-27.0	7.3-51.5
30 to 40 yr.	40	33 yr.	17.8	11.8-25.0	9.5-30.1	8.1-37.0
40 to 60 yr.	22	51 yr.	16.5	10.0-23.5	5.5-29.5	2.1-45.0
60 to 90 yr.	18	65.5 yr.	12.5	5.5-18.2	3.5-20.9	3.0-31.0

* The total number of observations was 375.

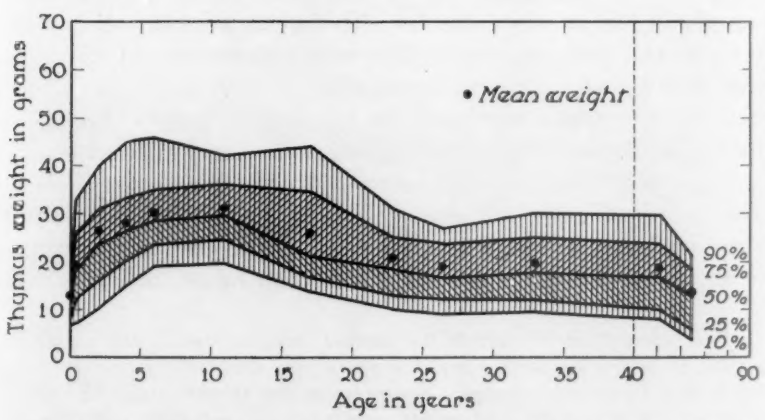

Chart 3.—Graphic standard of the normal thymus weight for age. The shaded zone represents the interquartile range of weight; the heavily shaded zone, the range in weight from the 10 to 90 percentile. The curve marked 50 per cent represents the median weights and the dots the mean weights. The broken line indicates a change in the age scale.

and 90 percentiles. Also, half of the thymuses are within the interquartile range of weight, one-fourth above it and one-fourth below it. Likewise, the middle 80 per cent of the weights is within the range from the 10 to 90 percentile, 10 per cent above and 10 per cent below it.

A single graphic chart for all ages was established by plotting each 10, 25, 50, 75 and 90 percentile given in table 2 against the median age of the group and joining all 10 percentiles by a continuous line, all 25 percentiles by another line, and so on for the 50, 75 and 90 per-

centiles, respectively.[43] On the resulting standard chart of normal thymus weight (chart 3), half the weights of glands from normal persons will be expected to fall within the shaded zone, or the interquartile range, one-fourth above and one-fourth below it, and 80 per cent will fall within the heavily shaded zone, 10 per cent above and 10 per cent below it.[44]

In order to measure the influence of the duration of illness in all diseases on the weight of the thymus, three standard graphs consisting of only the interquartile range and median were placed on a single chart. One of these charts was made for each disease category. The individual weights for "ill less than twenty-four hours" were plotted on the upper graph, for "ill from one to seven days" on the middle graph, and for "ill one week or more" on the lower graph. The charts for the diagnostic categories "accidents," "undetermined causes," "infections" and "miscellaneous causes" are given in charts 4, 5, 6 and 7, respectively.

Inspection of these charts shows that, whatever the cause of death, the weight of the thymus decreases with the length of illness, and this decrease is well under way in the first week. A measure of the degree of this decrease was obtained by counting on each graph the number of dots above, between and below the interquartile range. Because of crowding, the thymus weights for patients under 6 months were counted on a larger scale and the results were added to those counted on the graphs presented. For all diseases, when death took place within twenty-four hours of the onset of illness, 25 per cent of the weights were above, 48 per cent within and 27 per cent below the interquartile

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43. For constructing the graph the marked irregularities in the values for the 10 and 90 percentiles for the first five years were smoothed by one application of the method of moving average. For example, the 10 percentiles 6.5, 5.5 and 8.5 Gm. for the first three age periods were averaged and their mean 6.8 Gm. taken as the value for the second age period. By a continuation of this process, the values for the 10 percentiles became 10.2 Gm. for 1 to 3 years and 14.7 Gm. for 3 to 5 years, and for the 90 percentile, 32.8, 39.8 and 45.2 Gm. for the age periods 24 hours to 1 year, 1 to 3 years and 3 to 5 years, respectively.

44. In the beginning of this study I attempted to set up a similar graphic standard, using the mean plus and minus one, two and three probable errors. The data are sufficiently skew that the curve for minus three probable errors was at times less than zero grams and fell below the base line of the chart. Also I tested the reliability of the chart by plotting on it the actual weights from which it was constructed. The percentage of weights within the zone of the mean plus and minus one probable error was approximately 50, but the observed percentages for the zone of plus and minus two and three probable errors were not the expected 82 and 96. As a result, I resorted to the older and more limited method of percentiles to measure the dispersion of thymus weights. For all ages the medians are consistently below the means.

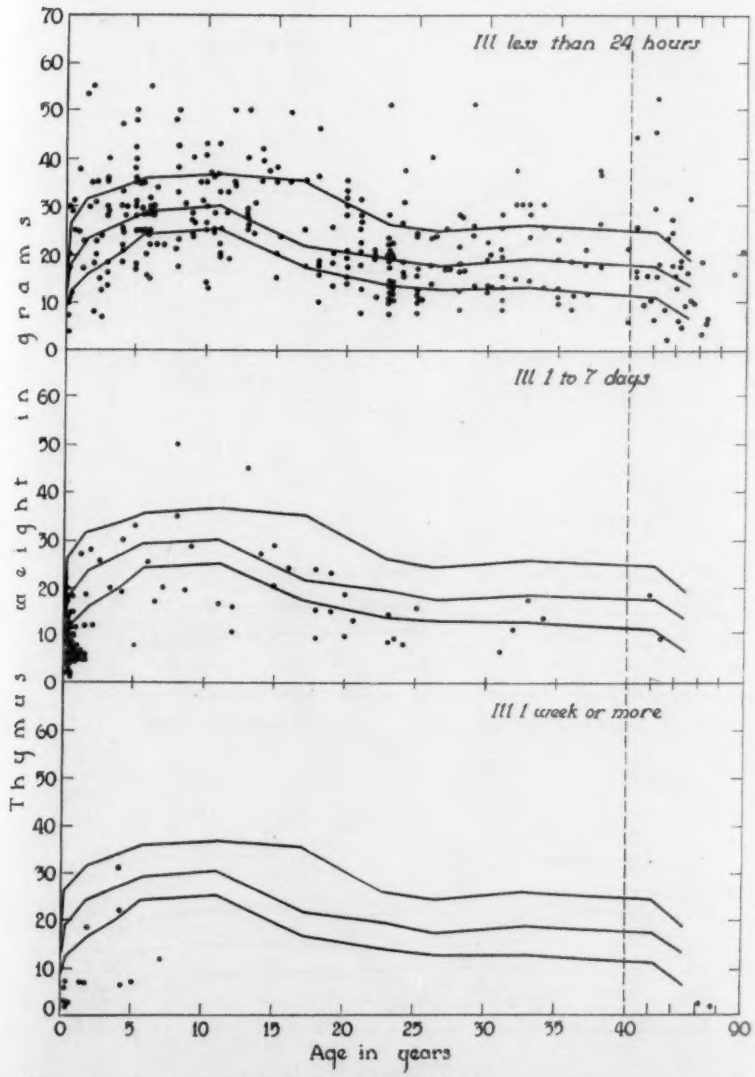

Chart 4.—A comparison of the individual thymus weights from "accidents," with the interquartile range of the normal graphic standard according to the duration of the illness. Thymus weights from infants under 3 days of age are not included on the graphs. (The standard graph, chart 3, was derived from the weights plotted in the upper graph.) The broken line indicates a change in the age scale.

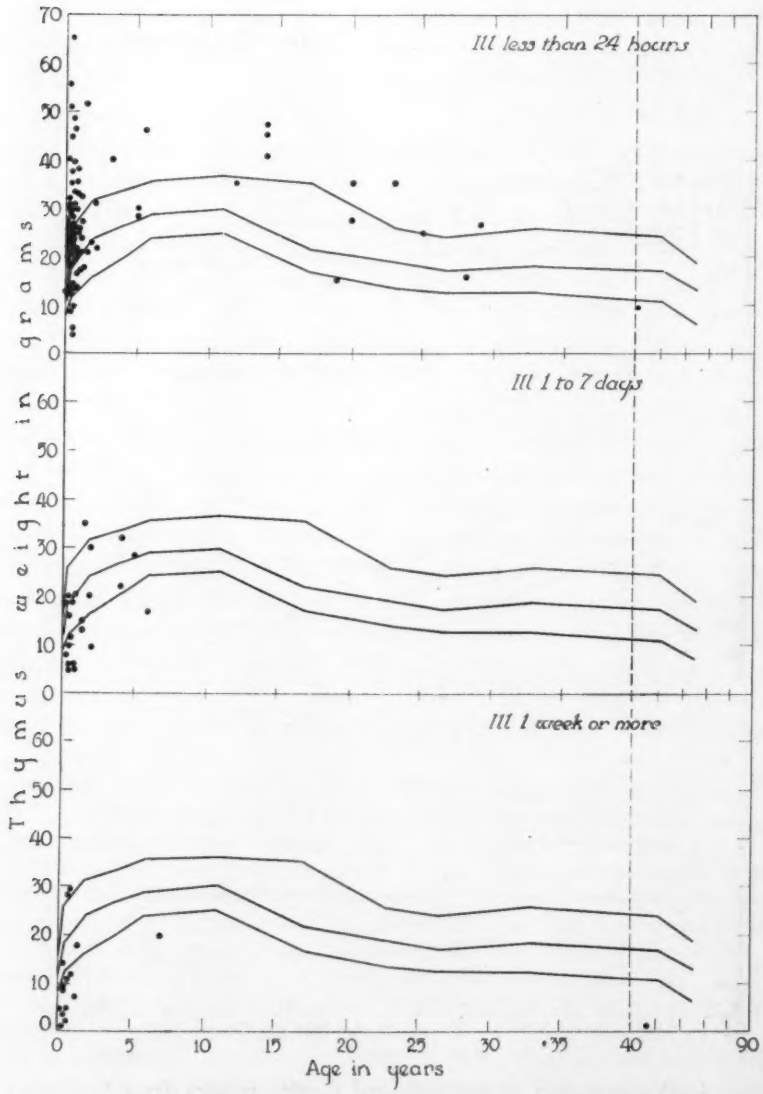

Chart 5.—A comparison of the individual thymus weights from "undetermined causes," with the interquartile range of the normal graphic standard according to the duration of the illness. Thymus weights for infants under 3 days of age are not included on the graph. The broken line indicates a change in the age scale.

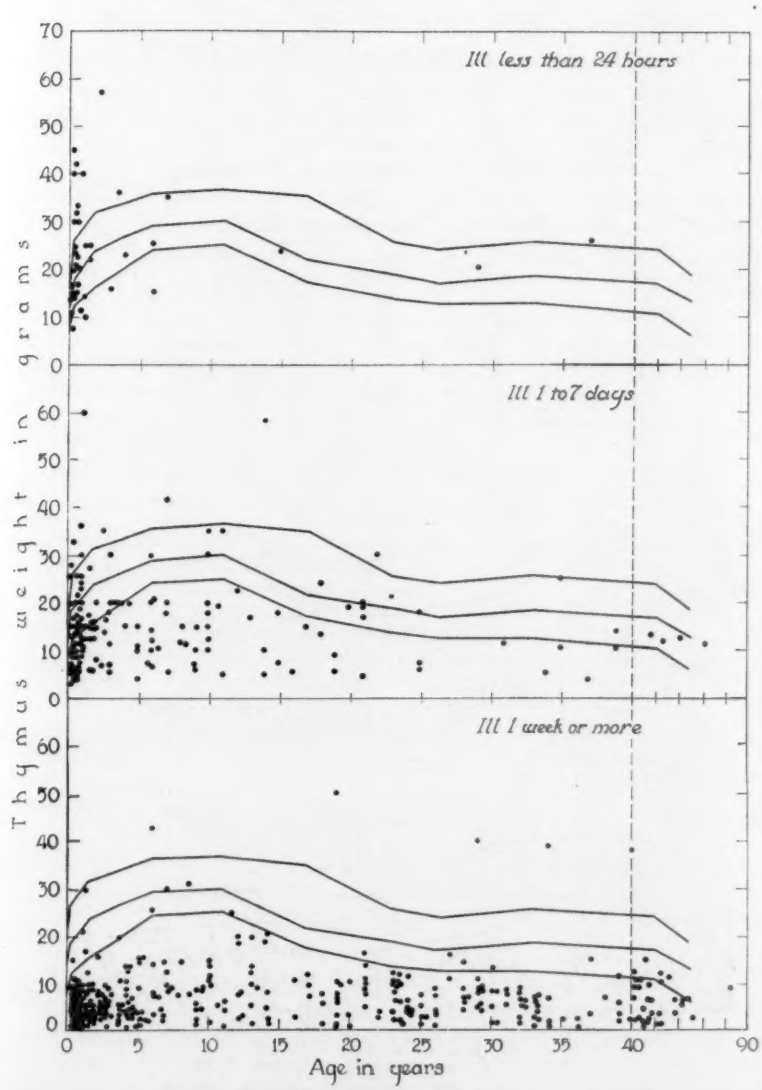

Chart 6.—A comparison of the individual thymus weights from "infections," with the interquartile range of the normal graphic standard according to the duration of the illness. Thymus weights from infants under 3 days of age are not included on the graph. The broken line indicates a change in the age scale.

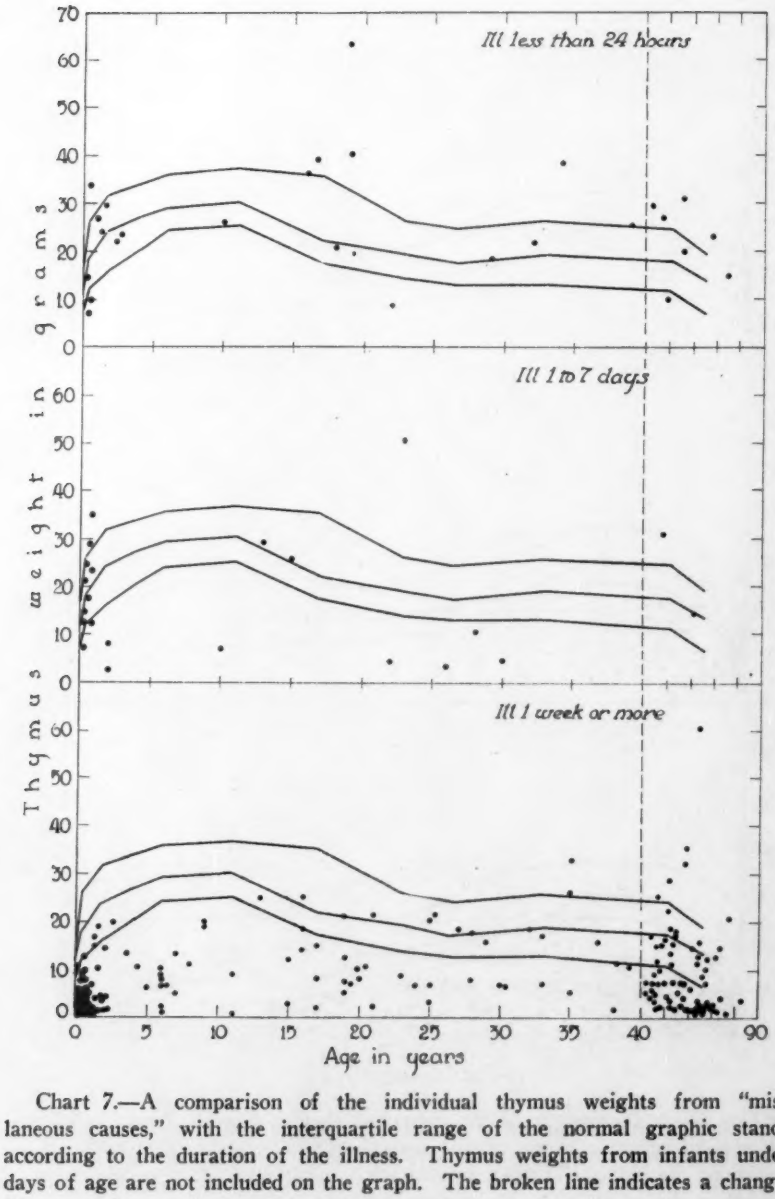

Chart 7.—A comparison of the individual thymus weights from "miscellaneous causes," with the interquartile range of the normal graphic standard according to the duration of the illness. Thymus weights from infants under 3 days of age are not included on the graph. The broken line indicates a change in the age scale.

range (table 3).[45] This result is in close agreement with the theoretical expectancy of 25, 50 and 25 per cent, respectively. Unexplained deaths, or status thymicolymphaticus if preferred, do not deviate from this trend. Surely this is adequate evidence that the size of the thymus has nothing to do with sudden death.[46] When illness has lasted from one

TABLE 3.—*Comparison of the Weights of the Thymus Glands in Various Pathologic Conditions According to the Duration of the Illness, with the Interquartile Range of the Normal Graphic Standard* *

	Ill Less Than 24 Hours				Ill from 1 to 7 Days				Ill 1 Week or More			
		Percentage				Percentage				Percentage		
	No. Cases	Above	Within	Below	No. Cases	Above	Within	Below	No. Cases	Above	Within	Below
Theoretical expectancy	..	25	50	25	..	25	50	25	..	25	50	25
Accidents	..	..	..	..	95	7	35	58	16	0	25	75
Undetermined causes	157	27	54	19	47	2	32	66	30	3	17	80
Infections	53	21	47	32	195	6	25	69	488	1	5	94
Congenital defects	21	19	43	38	25	4	32	64	32	0	6	94
Miscellaneous causes	38	32	47	21	54	7	37	56	203	4	22	73
Total	269	25	48	27	416	6	30	64	769	2	11	87
Exophthalmic goiter									46	59	26	15
Leukemia									16	25	25	50

* The total number of observations was 1,516.

Comparison of Means and Coefficients of Variation

Age Interval	Accidents		Undetermined			Diff.
	No. Cases	M ± P.E. (C.V. ± P.E.)	No. Cases	M ± P.E. (C.V. ± P.E.)	Diff. ± P.E.	P.E.
Birth to 24 hr.	56	12.7 ± 0.5 (43.3 ± 3.3)	43	11.0 ± 0.6 (50.8 ± 6.0)	−1.7 ± 0.8 (+7.5 ± 6.8)	2.1 (1.1)
1 day to 1 yr.	67	19.3 ± 1.9 (48.7 ± 8.9)	89	22.7 ± 0.8 (52.5 ± 3.3)	+3.4 ± 2.1 (+3.8 ± 9.5)	1.6 (0.4)
1 to 5 yr.	36	27.0 ± 1.4 (45.9 ± 4.4)	10	28.9 ± 2.2 (34.0 ± 6.0)	1.9 ± 2.6 (−11.9 ± 7.4)	0.7 (1.6)

45. Because of the few cases of congenital defects, the graphs for them are not reproduced, but the results of the counts are included in table 3.

46. The lack of any difference between the normal thymuses and those occurring in "status lymphaticus" was redemonstrated by finding no significant difference between their mean weights and coefficients of variation for the first three age periods. Definition of the symbols and the method of interpreting the differences are given in table 5. Greenwood (footnote 13) in a similar analysis of Hammar's data, obtained a significant difference between the coefficient of variation 22.49 ± 2.17 for normals and the coefficient 44.31 ± 4.22 for "abnormals." On recalculation, the coefficient for normals was found to be 31.07 ± 3.76. The corrected difference between the normal and "abnormal" weights is not significant. Incidentally, the corrected difference agrees with Greenwood's general point of view.

to seven days, the weights have decreased until 64 per cent instead of the expected 25 per cent are below the interquartile range, and when the illness lasted one week or more, 87 per cent instead of 25 per cent.

The only exceptions to this rule occur in exophthalmic goiter and leukemia [47] (chart 8). In the former, even though the subjects had usually lost weight and had been ill several months or years, 59 per

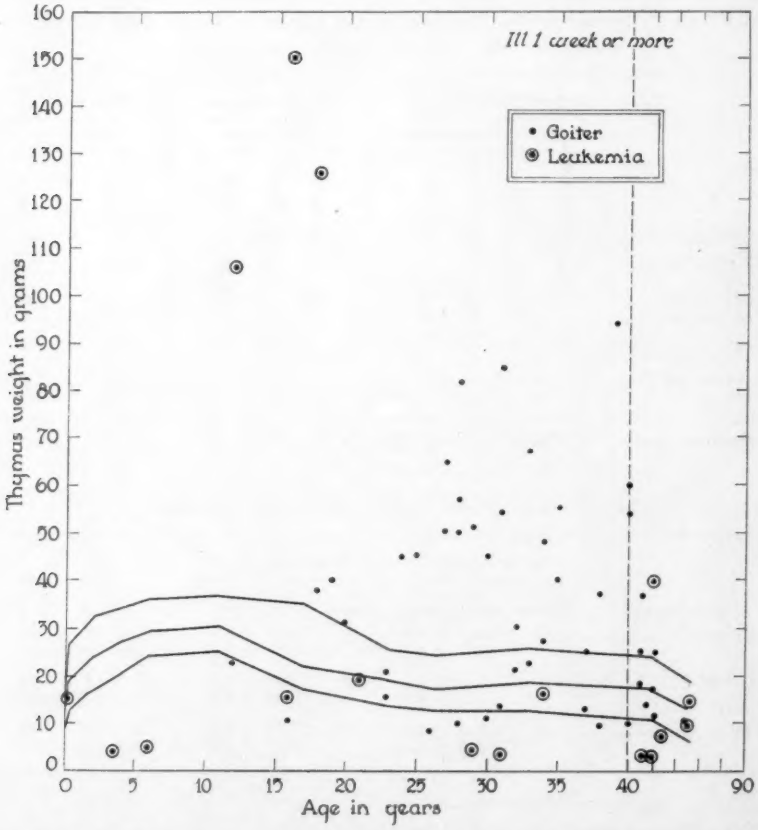

Chart 8.—A comparison of the individual thymus weights from "exophthalmic goiter and leukemia," with the interquartile range of the graphic standard. The broken line indicates a change in the age scale.

cent were above, 26 per cent between and only 15 per cent below the interquartile range. Moreover, six weights, or 13 per cent, were above the maximum weight of 55 Gm. found in the normal group. Accord-

47. Tumors of the thymus of course do occur, but none was reported in this series. A recent report has been published by H. M. Margolis (Tumors of the Thymus: Pathology, Classification and Report of Cases, Am. J. Cancer **15**: 2106, 1931).

ing to this, then, the thymus may truly be called hypertrophied in many cases of exophthalmic goiter. In leukemia, however, the results indicate that a few glands that show lymphatic infiltration are enormous, while others show the general effect of inanition and are below median size.

In short, most diseases cause an involution of the thymus which begins by the second day of illness and is so advanced by the second week of illness that approximately 90 per cent of the glands fall below the lowest quartile of the normal weight range. The reader can readily estimate the degree of involution caused by any given disease by plotting on this standard either the thymus weights of his subjects or those given in table 1 and Hammar's monographs. On the whole, one will

TABLE 4.—*Incidence of Good and Poor Nutrition According to the Cause of Death and the Duration of the Illness* *

Cause of Death	Ill Less Than 24 Hours.			Ill from 1 to 7 Days			Ill 1 Week or More		
		Nutrition			Nutrition			Nutrition	
	No. Cases	Good, per Cent	Poor, per Cent	No. Cases	Good, per Cent	Poor, per Cent	No. Cases	Good, per Cent	Poor, per Cent
Accidents	311	86	14	75	83	17	11	36	64
Undetermined causes	125	82	18	47	51	49	27	33	67
Infections	41	78	22	157	68	32	423	33	67
Congenital defects	20	70	30	24	46	54	27	22	78
Miscellaneous causes	32	94	6	44	68	32	167	32	68
Exophthalmic goiter	..	..	..	..	..	..	23	22	78
Leukemia	..	..	..	..	..	..	12	50	50
All causes	529	84	16	347	67	33	690	32	68

* The total number of observations was 1,566.

find that the wasting diseases such as cancer and tuberculosis cause the greatest reduction in the weight of the thymus, and diseases not associated with marked inanition the least.

This reaction to inanition is not limited to the thymus, for most organs of the body are reduced in size during inanition. According to Jackson's summary [1] of the effects of inanition, the thymus, lymphoid tissue and subcutaneous fat react more quickly and markedly to starvation than other parts of the body. In these data, for example, when death took place within twenty-four hours of the onset of illness, 84 per cent of the subjects were well nourished, while after from one to seven days only 67 per cent and after one week only 33 per cent were well nourished (table 4). As stated before, my personal impression from performing necropsies was that when illness had lasted a week or more most of the lymphoid tissue like the thymus had shifted from a prominent to an inconspicuous state, but the regional lymph nodes of the diseased part had become swollen, congested and conspicuous.

STATISTICAL COMPARISON

In previous studies of normal thymuses, i. e., those from persons dying of readily demonstrable causes within one or two days of the onset of illness, the mean instead of the median [44] was used as the measure of "normal size." Greenwood and Woods [13] and Young and Turnbull [15] estimated the dispersion of weight for both their own data and Hammar's by the coefficient of variation.[48] Hammar himself measured the variability by an arbitrarily established system of "quarters." [49]

To compare the data of the present study with the reviewed studies, the means and coefficients of variations were calculated for all age periods. Comparisons between the statistical constants are limited to those of this study and those of the studies of Greenwood and Woods [13] and of Young and Turnbull,[15] since this study includes Hammar's [9] data and Greenwood and Woods' data are essentially the same as Bratton's.[12] The results for all three studies are given in table 5 along with the differences between the mean and coefficients of variation and the probable errors of these differences.

In current statistical parlance, when the difference between two statistical constants, such as the means of two arrays, is three or more times its probable error, this difference is considered significant.[50] The basis for this assumption is that when the ratio (i. e., the difference divided by its probable error) is 3, such a difference could occur by chance only about 5 times in 100, hence the difference is probably real and not merely apparent. The cause of the difference must, of course, be sought for in the selection and character of the original data.

According to these criteria (columns 12 and 13 and 19 and 20 of table 5), except for the fetal period and infancy, the means of the two previous English studies are usually smaller than those for this study, but are not significantly smaller. On the other hand, the coefficients of variation are usually larger, but only occasionally are significantly larger. Slight differences in selecting normal data, since the

48. If the data follow a normal distribution curve, 68 per cent of the weights should fall within the weight range of plus and minus one coefficient of variation (or one standard deviation) from the mean. Since the distribution of these data is usually skewed, this prediction is unreliable.

49. Hammar considered the average between the minimum and mean weight the upper limit of the first quarter, the mean that of the second quarter, the average of mean and maximum that of the third quarter, and the maximum that of the fourth quarter. P. H. Guttman (Addison's Disease, Arch. Path. **10**:742 and 895 [Nov.-Dec.] 1930) used a graphic standard of normal thymus weight plotted from these "quarters."

50. Any standard textbook of statistical methods gives a technic for calculating these statistics. In this study I followed the technic given by H. L. Dunn (Application of Statistical Methods in Physiology, Physiol. Rev. **9**:275, 1929).

TABLE 5.—*Comparison of the Mean Weights and Coefficients of Variation of Normal Thymuses in the Present Study with Those of Previous Studies**

TABLE 5.—*Comparison of the Mean Weights and Coefficients of Variation of Normal Thymuses in the Present Study with Those of Previous Studies* *

	Present Study†					Greenwood and Woods†							Young and Turnbull†						
										Diff.							Diff.		
Age Interval	No. Cases	Mean Age	M ± P.E. (C.V. ± P.E.)	SD	Age Interval	No. Cases	Mean Age	M ± P.E. (C.V. ± P.E.)	SD	Diff. ± P.E.	P.E.	P.	No. Cases	Mean Age	M ± P.E. (C.V. ± P.E.)	SD	Diff. ± P.E.	P.E.	P
Term fetuses‡	80		10.7 ± 0.3 (42 ± 2.6)	4.5	Term fetuses	52		10.3 ± 0.5 (47 ± 3.7)	4.8	−0.4 ± 0.6 (+5.0 ± 4.5)	0.7 (1.1)	63 (46)	31		21.8 ± 1.6 (59 ± 6.6)	12.8	+11.1 ± 1.6 (+17 ± 7.1)	6.9 (2.4)	>1 (11)
Birth to 24 hr.§	56		12.7 ± 0.5 (43 ± 3.3)	5.5															
24 hr. to 1 yr.	11	1.9 mo.	19.3 ± 1.9 (49 ± 8.9)	9.4													+ 5.5 ± 2.2 (+ 3 ± 9.8)	2.5 (0.3)	9 (84)
Birth to 1 yr.	67	10 days	14.0 ± 0.6 (48 ± 3.4)	6.7	Birth to 1 yr.	71	2.2 mo.	14.1 ± 0.6 (54 ± 3.8)	7.7	+0.1 ± 0.8 (+6 ± 5.1)	0.1 (1.2)	94 (54)	56	3 mo.	24.8 ± 1.2 (52 ± 4.1)	12.8	+10.8 ± 1.3 (+ 4 ± 5.3)	8.3 (0.8)	>1 (59)
1 to 3 yr.	17	1.9 yr.	26.3 ± 2.3 (53 ± 7.9)	13.9															
3 to 5 yr.	19	3.5 yr.	27.7 ± 1.3 (31 ± 3.8)	8.5															
1 to 5 yr.	36	2.7 yr.	27.0 ± 1.4 (46 ± 4.4)	12.4	1 to 6 yr.	90	2.9 yr.	23.5 ± 0.6 (36 ± 2.0)	8.5	−3.5 ± 1.5 (−10 ± 4.8)	2.3 (2.1)	12 (16)	65	3.5 yr.	23.3 ± 0.9 (44 ± 3.1)	10.4	− 3.7 ± 1.7 (+ 2 ± 5.4)	2.2 (0.4)	13 (78)
5 to 10 yr.	52	6.4 yr.	30.5 ± 0.9 (30 ± 2.2)	9.2	6 to 11 yr.	41	7.7 yr.	29.2 ± 1.3 (41 ± 3.5)	11.9	−1.3 ± 1.6 (+11 ± 4.1)	0.8 (2.7)	59 (7)	70	7.8 yr.	28.7 ± 0.9 (37 ± 2.4)	10.7	− 1.8 ± 1.3 (+ 7 ± 3.3)	1.4 (2.1)	35 (16)
10 to 15 yr.	40	11.5 yr.	31.1 ± 0.9 (28 ± 2.3)	8.7	11 to 16 yr.	18	13.3 yr.	30.4 ± 1.3 (27 ± 3.3)	8.3	−0.7 ± 1.6 (−1 ± 4.0)	0.4 (0.3)	78 (84)	55	13.6 yr.	33.9 ± 1.3 (43 ± 3.2)	14.6	+ 2.8 ± 1.6 (+15 ± 3.9)	1.8 (3.8)	23 (1)
15 to 20 yr.	20	17.6 yr.	25.7 ± 1.7 (44 ± 5.7)	11.3	16 to 21 yr.								35		21.3 ± 1.3 (55 ± 5.6)	11.7	− 4.4 ± 2.1 (+11 ± 8.0)	2.1 (1.4)	16 (35)
20 to 25 yr.	50	22.3 yr.	20.5 ± 0.8 (41 ± 3.2)	8.3	21 to 26 yr.								29		18.4 ± 1.5 (64 ± 7.6)	11.7	− 2.1 ± 1.7 (+23 ± 8.2)	1.2 (2.8)	54 (6)
25 to 30 yr.	30	27.1 yr.	19.3 ± 1.1 (47 ± 5.0)	9.1	26 to 31 yr.								22		14.9 ± 1.4 (67 ± 9.4)	9.9	− 4.4 ± 1.8 (+20 ± 10.6)	2.4 (1.9)	11 (19)
30 to 40 yr.	40	33.6 yr.	19.7 ± 0.9 (43 ± 3.9)	8.5	31 to 36 yr.								17		14.8 ± 1.6 (64 ± 10.1)	9.5	− 4.9 ± 1.8 (+21 ± 10.8)	2.7 (1.9)	7 (19)
40 to 60 yr.	22	49.9 yr.	18.7 ± 1.6 (59 ± 8.0)	11.0	36 to 46 yr.								25		14.2 ± 1.2 (62 ± 7.9)	8.7	− 4.5 ± 2.0 (+ 3 ± 11.2)	2.3 (0.3)	12 (84)
					46 to 56 yr.								28		15.3 ± 1.3 (65 ± 8.0)	10.0	− 3.4 ± 2.1 (+ 6 ± 11.3)	1.6 (0.5)	27 (73)
60 to 90 yr.	18	67.2 yr.	13.4 ± 1.2 (55 ± 8.1)	7.4	56 to 66 yr.								16		12.7 ± 1.5 (69 ± 11.5)	8.8	− 0.7 ± 1.9 (+14 ± 14.1)	0.4 (1.0)	78 (50)
					66 yr. and over								13		9.4 ± 1.5 (83 ± 17.0)	7.9	− 4.0 ± 1.9 (+28 ± 18.8)	2.1 (1.5)	16 (23)

* The total number of observations in the present study was 455; in Greenwood and Woods' study, 272, and in Young and Turnbull's study, 462.

† M ± P.E. indicates the mean thymus weight in grams and its probable error; C.V. ± P.E., the coefficient of variation and its probable error; SD, the standard deviation; Diff. ± P.E., the difference between two means or coefficients and its probable error; Diff./P.E. the ratio of difference and its probable error. When the ratio is 3 or more, the difference is probably significant. P indicates the chances in 100 that the difference occurred from sampling.

‡ Limited to fetuses measuring from 48 to 52 cm. in total body length.

§ Mean total body length, 50.4 cm.

thymus is so sensitive to inanition, could readily account for this tendency of the English weights to be both lighter and more variable.[51] Also, the age groups used by the English workers and those in this study are slightly different, as can be seen in table 5.[52]

The significant differences in infancy between the mean 24.8 Gm. obtained by Young and Turnbull and the means 14 and 14.1 Gm. obtained in the other two studies are probably due to a disproportionate number of new-born infants in the latter studies. This is demonstrated by finding no significant difference between 24.8 Gm., the mean of Young and Turnbull, and the mean 19.3 Gm. obtained for this series when all infants under 24 hours of age are omitted.

The similarly large significant difference for full term fetuses between the mean 21.8 Gm. obtained by Young and Turnbull and the means 10.7 and 10.3 Gm. obtained in the other two studies is probably due to an artificial inclusion of postmature fetuses.[53] This supposition is supported by several findings: 1. Lomer[54] found the same weight, 21.6 Gm., for postmature fetuses weighing from 4,000 to 5,000 Gm. 2. According to the thymus weight-body length formula[55] developed for the fetal period by Scammon, the thymus weighs 11 Gm. when the total body length is 50 cm. and 21 Gm. when the total body length is 59 cm.[56] 3. In an initial analysis of the Minnesota data,

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51. In all three studies the differences between normal male and female thymus weights were usually not significant. In this study the weights for females were too few for the results to be conclusive.

52. Since the ages given in necropsy protocols are at best only rough approximations, the slight differences in the age groups, usually 1 year, did not seem to justify either rearranging the data or correcting statistically for differences in age. Parents usually give the age according to the last birthday, although this folk custom is being modified by the custom of insurance companies, schools and the like, which request the age to the nearest birthday. Attending physicians, distant relatives and acquaintances commonly give such replies as about 40, almost 60 and not over 50.

53. A possible factor causing an artificial selection of term fetuses is the common custom of physicians to call mature all infants not premature, as the postmature infant does not need special care. Also in a preliminary analysis of causes of stillbirths and neonatal deaths, Dr. Adair, working at this university, found the proportion of postmature infants among all neonatal deaths higher than the proportion in all births.

54. Lomer: Ueber Gewichtsbestimmungen der einzelnen Organe Neugeborener, Ztschr. f. Geburtsh. u. Gynäk. **16**:106, 1889.

55. $T\ W = 0.000001312\ L^{4.0654}$ when T W equals the thymus weight in grams and L equals the body length in centimeters. In Scammon's original report (footnote 18) the coefficient was given incorrectly as a seven place decimal instead of the correct nine place decimal reported here.

56. The average total body weight and the length at term, i. e., ten lunar months, are commonly found to be 3,000 Gm. and 50 cm., respectively.

217 fetuses were arranged by 2 or 3 cm. intervals of total body length. Fetuses measuring from 48 to 50 cm. were considered mature; those measuring less, premature; and those measuring more, postmature (table 6). The mean thymus weight, 10.3 Gm., for term fetuses obtained by Greenwood and Woods is not significantly different from the means, 9.1 and 11.6 Gm., for mature fetuses, but is significantly larger than the mean, 7.6 Gm., for premature fetuses and significantly smaller than the means, 13.1, 13.2 and 17.6 Gm., for postmature fetuses. Apparently Greenwood and Woods' definition of full term is equivalent to the one used in this study. In contrast, the mean thymus weight of 21.8 Gm. found by Young and Turnbull is larger than the means for premature, mature and postmature fetuses, but is not significantly larger than the mean for markedly postmature fetuses measuring from 56 to 58 cm. Hence their fetuses may be considered postmature; however, since they gave no information from which maturity can be judged, the evidence that their fetuses were predominately postmature remains circumstantial.

TABLE 6.—*Comparison of Mean Thymus Weights for Fetuses in the Present Study with Those of Term Fetuses in Previous Studies* *

	University of Minnesota			Greenwood and Woods (M ± P.E. = 10.3 ± 0.45)			Young and Turnbull (M ± P.E. = 21.8 ± 1.55)		
Maturity	No. Cases	Body Length Intervals, Cm.	M ± P.E.	Diff. ± P.E.	Diff./P.E.	P.	Diff. ± P.E.	Diff./P.E.	P.
Premature	27	45 to 48	7.6 ± 0.46	+2.7 ± 0.64	4.2	>1	+14.2 ± 1.62	8.8	>1
Mature	29	48 to 50	9.1 ± 0.44	+1.2 ± 0.63	1.9	19	+12.7 ± 1.61	7.9	>1
	51	50 to 52	11.6 ± 0.47	−1.3 ± 0.65	2.0	18	+10.2 ± 1.62	6.3	>1
Postmature	50	52 to 54	13.1 ± 0.46	−2.8 ± 0.64	4.4	>1	+8.7 ± 1.62	5.4	>1
	44	54 to 56	13.2 ± 0.49	−2.9 ± 0.67	4.3	>1	+8.6 ± 1.63	5.3	>1
	16	56 to 58	17.6 ± 0.94	−7.3 ± 1.04	7.0	>1	+4.2 ± 1.81	2.3	12

* In this table M ± P.E. indicates the mean thymus weight in grams and its probable error; Diff. ± P.E., the difference between two means and its probable error; Diff./P.E., the ratio of the difference to its probable error. When the ratio is 3 or more, the difference is probably significant. P. indicates the chances in 100 that such a difference occurred from sampling.

The comparisons in table 5 indicate that, on the whole, the thymuses used in this study have approximately the same mean size and dispersion of weights as those used by previous workers. Hence, the data used in this study are essentially the same as those used in previous studies of the weights of thymuses from normal persons dying shortly after the onset of illness of readily demonstrable causes other than "status thymicolymphaticus."

SUMMARY

This analysis has again demonstrated that while the mean thymus weight in normal persons is about 2 Gm. more than the median, both increase rapidly in the first months of life, double their birth size by

2 years and triple it by 11 years; then both decrease slowly to about birth size in senility. This general progression holds for data from the United States, Germany, France, Sweden and England.

A graphic presentation of Hammar's data indicates that the parenchyma decreases sufficiently after puberty to lower the total weight of the thymus even though the connective tissue and fat are increased in amount.

At all ages the variability of the weight of the thymus is high. This dispersion has been estimated both by interquartile range and by coefficient of variation. Since the spread of weights above the median weight is greater than that below it, the interquartile range has been used to construct a graphic standard of normal variability, instead of the standard deviation or a related statistic.

When illness has lasted longer than twenty-four hours, the weight of the thymus is reduced regardless of the cause of death, with the exception of tumors of the thymus, leukemia and exophthalmic goiter. This involution is probably part of the general involution of most organs found in inanition, but the thymus, like the subcutaneous fat and lymphoid tissue, reacts markedly and rapidly, so that all three are significantly decreased in most illnesses lasting more than twenty-four hours.

The concept of a pathologic state arose from misconstruing the normal prominent thymus and lymphoid tissue for a constitutional abnormality and vice versa, the involuted, inconspicuous thymus of inanition being misconstrued for the normal.

Pediatric Biographies

HUGH DOWNMAN

1740-1809

JOHN RUHRÄH, M.D.
BALTIMORE

Hugh Downman was born in 1740 at Newton House, Exeter. He was educated first in the Exeter grammar school and then at Balliol College, Oxford, where he was sent in 1758, and from which he

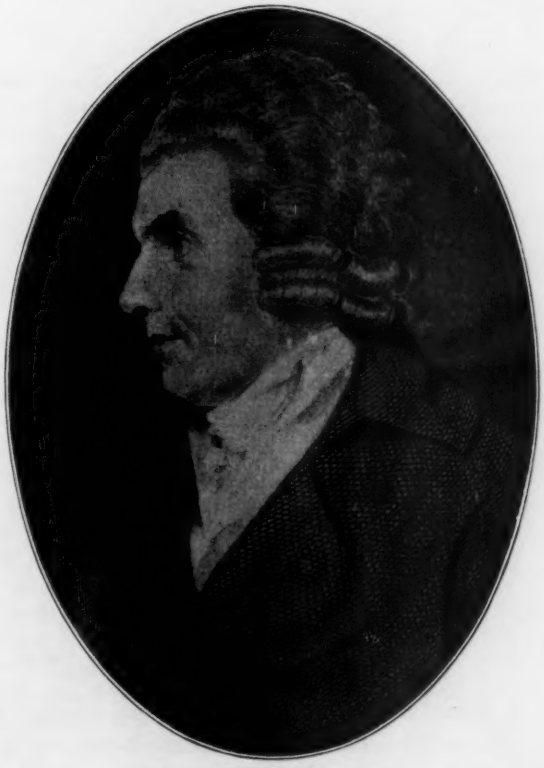
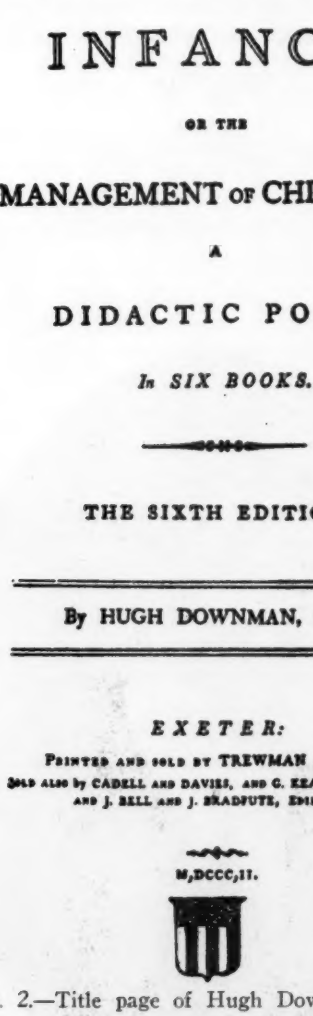


Fig. 1.—Hugh Downman.

received his B.A. degree in 1763. He was ordained the same year in Exeter Cathedral and then went to Edinburgh for his medical education. While there, he boarded with the blind poet, Thomas Blacklock.

This association may have had some influence on his subsequent devotion to poetry. In 1769, he went to London for clinical experience in the hospitals. After receiving an M.A. degree at Jesus College, he returned to Exeter, where he practiced about eight years. Ill health



INFANCY,

OR THE

MANAGEMENT OF CHILDREN:

A

DIDACTIC POEM,

In SIX BOOKS.

THE SIXTH EDITION.

By HUGH DOWNMAN, M. D.

EXETER:

PRINTED AND SOLD BY TREWMAN AND SON;

SOLD ALSO by CADELL AND DAVIES, AND G. KEARSLEY, LONDON;

AND J. BELL AND J. BRADFUTE, EDINBURGH.

M,DCCC,II.

Fig. 2.—Title page of Hugh Downman's poem.

caused him to retire, but twelve years later he resumed active work. Subsequently, he was forced to give up his practice on account of his health, and he died on Sept. 23, 1809.

Downman was regarded as an able physician, but he was also widely known as a man of letters; he founded a literary society in Exeter and wrote much on a great variety of topics. In 1768, he published a poem, "The Land of the Muses." He wrote a number of plays, a

volume of which was printed in 1792, but as a playwright he was not much of a success. One play was called "Lucius Junius Brutus"; another, "Belisarius," ran a few nights in a theater in Exeter, and another, "Edith, a Tragedy," ran sixteen nights. He helped in the translation of Voltaire for the English edition of 1781. He wrote many poems, which were collected and reprinted in several editions; some were published with critical notes by an unknown author. His best known poem is "Infancy, or the Management of Childhood." This was originally published in quarto form in three separate parts, 1774, 1775 and 1776, in London. Seven editions were printed during his life, which is sufficient evidence of its popularity at that time.

It is a long poem and not too exciting reading, but viewed in its relation to the history of pediatrics and of infant welfare it takes on a certain interest. There are six books. The argument of the first and two extracts must suffice to illustrate the scope and style of the poem.

ARGUMENT

The Invocation and Introduction. Health is the greatest blessing of mankind. —It should be the chief aim of parents to procure their children the enjoyment of it.—Nature and instinct therefore are to be followed.—Pernicious custom of giving children some drug soon after they are born.—The best remedy, at that time, is the first milk of the mother.—Various reasons and motives for the mother's suckling her children.—An amiable duty.—Apostrophe to tender affection.—Directions how to choose a nurse, if the mother can not perform that office herself.—Cities destructive to infants. Recommendation of the country.—The mother should oversee the conduct of the nurse.—The nurse's usual manner of life should be altered as little as possible.—Address to Habit.

Because the child, with reason unendow'd
And power of speech, by words to express his grief
Nature permits not; some believe the source
Of anguish and affections is conceal'd
From every eye, and deem assistance vain.
Or to the nurse, or vaunting midwife trust,
Who cases manifold and similar
Have oft beheld, and never fail'd to cure:
For each her nostrum boasts; if harmless this,
And trifling, it were well, did not the wing
Of time speed fast the irrevocable hour
Of wish'd redress. But frequently the drug
They praise, the cordial draughts are fraught with death,
Hurrying convulsions on of direst kind;
Or with narcotic venom strong embued,
Plunging the patient in eternal sleep.
Yet nature, in thy child, *tho'* not in words,
Speaks plain to those who in her language vers'd
Justly interpret. Are the different tones
Of woe unfaithful sounds? Can he, whose sight
Hath traced the various muscles in their course,

When irritated in the different limbs,
Retracted, or extended, or supine,
Fix no conclusions on the seat of pain?
Is it of no avail to mark the breath,
How drawn? the face? the motions of the eye?
The salient pulse? the eruptions on the skin?
The skin itself, constricted or relaxed?
The mode of sleep? of waking? heat? or thirst?
From which, and numerous traits beside arranged,
Combined, abstracted, and maturely sigh'd,
Judgment its practice forms? Are characters
Like these which ask the nice decyphering soul,
Intelligible to beldames old,
Who wrapped in darkness, utter prophesies
And lying oracles, which cheat the ear
Or followed, to destruction lead the way?
Oh! may good angels, kindling in thy breast
The lamp of reason, guard thee from their snares!
Blind guides assiduous to deceive the blind.
But, now with idle terrors do we seek
To wound affection, from experience taught
We know what medicines, different in effect,
And opposite, the varying symptoms claim.
Antiphlogistics which the vital heat
Increased, depress; and Cardiacs which excite;
And Opiate Sedatives, in vulgar hands
Pernicious as the deadly nightshade's juice,
And Drastics, which consummate spell along,
And wise discretion, when the moment calls,
Should dare advise.

Another short part about the lymph nodes is well worth quoting:

The wild delusions which the source affords,
With silent scorn or pity had the muse
Often attested. The luxuriant glands,
In infants stiled of disproportion'd size,
And the two copious fluids, they secern,
Or tough and viscid, some alone condemn.
As if these glands by nature were ordain'd
So large without design, or worse, to prove
The cisterns of disease. Acidity
Some only blame; and some the sting severe
Of acrimonious humours. These accuse
The noisome worm, however hid from sight
Those, as exciting fever, reprobate
Nought but the growing teeth. Repletion some.
While others dreadful fits survey within,
Or e'en pretend to trace them in the smile
Of downy sleep. Nor women solely err.
The pedant has his whims; and he the light
Fantastic form, who superficial skims
The froth of science, yet would fain appear

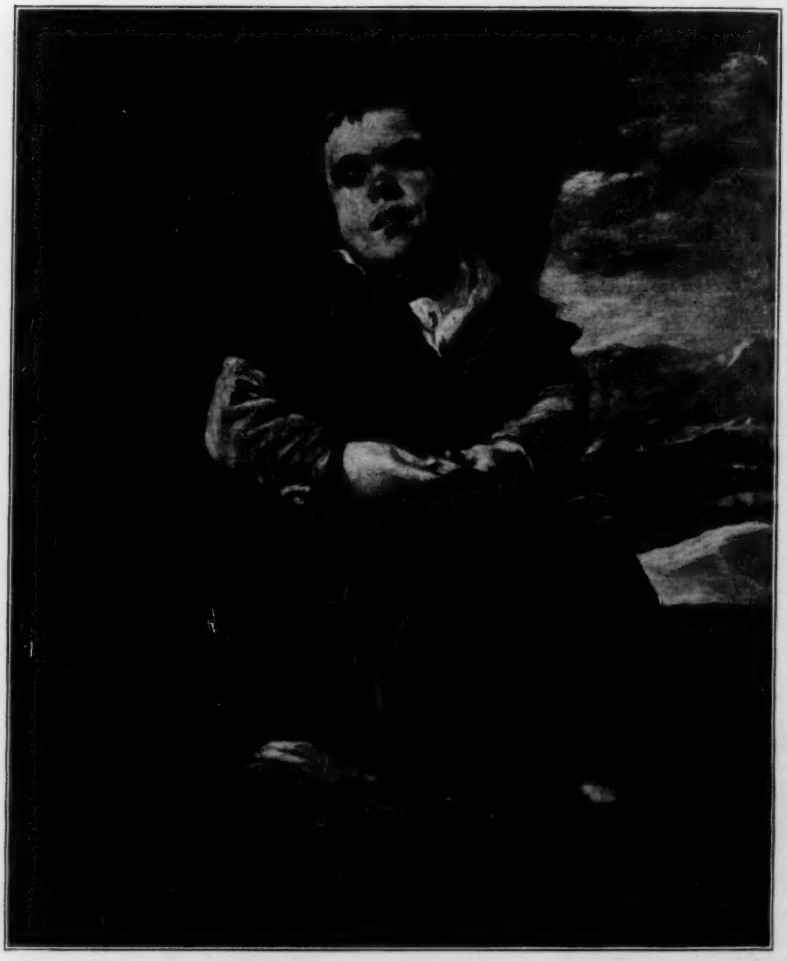
Most intimate in its profoundest depths;
Now a phenomenon beholds, to which,
Like the first man, intuitively wise,
He cannot give a name. What strange conceits
Have not philosophers embraced, intent
The principles of Galen to defend!
Or to deduce from chymic elements
Recondite causes! Or the line supply
And mathematic rule, to buildings raised
On mere imaginary ground? Or search
The moon, then aspects of the different stars!
While some, from animated beings, thick
Diffused through space, invisibly minute,
Have every ill derived, tormenting man.

Pediatrics in Art

MENTAL DETERIORATION

JOHN RUHRÄH, M.D.
BALTIMORE

Velázquez, Diego Rodriquez de Silva, left a number of paintings of medical interest. El Niño de Vallecas, or the child of Vallecas, is one of these. Here one sees a typical idiot, showing all the stigmas of central



El Niño de Vallecas.

degeneration of the nervous system. The nucleus of the third nerve has been affected, as shown in the right eye. The right side of the face is flattened; the body and extremities are short and undeveloped. This is one of the best examples of idiocy depicted by an artist. The photograph is by Hanfstaengl, Munich. The original painting is in the Museo du Prado at Madrid.

News and Comment

UNIVERSITY NEWS

The faculty of the New York Post-Graduate Medical School and Hospital of Columbia University announce the appoint of Dr. Roger H. Dennett as professor of pediatrics.

GENERAL

Benjamin Knox Rachford Lectures.—The second annual series of the Benjamin Knox Rachford Lectures in Cincinnati was given April 22 and 23 by Dr. Bronson Crothers, assistant professor of pediatrics of Harvard University Medical College.

Staff Changes.—Dr. Fritz B. Talbot has resigned as chief of staff of the pediatric department of the Massachusetts General Hospital, Boston, and has been succeeded by Dr. Harold L. Higgins of Boston.

Bequests and Donations.—St. Christopher's Hospital for Children, Philadelphia, was bequeathed $1,000 by the will of Gustave Rumpf.

Montgomery Hospital, Norristown, Pa., was left $50,000 to finance a children's ward in a new hospital by the will of John Hoffman, Jr.

The Children's Free Hospital and Kosair Crippled Children's Hospital, Louisville, Ky., will eventually receive half of the $300,000 estate of Edward A. Hewett.

The Children's Mercy Hospital, Kansas City, Mo., was given $10,000 by the will of Mrs. P. A. Seitz.

PERSONAL

Dr. J. D. Leebron has been appointed pediatrist to the Northern Liberties Hospital. His service will include a department for the prevention of diseases in children.

CORRECTION

In the article by Drs. James M. Baty, Kenneth D. Blackfan and Louis K. Diamond, entitled, "Blood Studies in Infants and in Children: I. Erythroblastic Anemia; a Clinical and Pathologic Study," in the March issue (**43**:667, 1932), the word "not" in the last line of the first paragraph on page 670 should be eliminated, making the sentence read:

"The changes in the blood picture following removal of the spleen *were* given."

Correspondence

"ANEMIA OF THE NEW-BORN"

To the Editor:—In his article entitled "Anemia of the New-Born," in the February, 1932, issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN, page 337, Dr. Arthur F. Abt, after reviewing the fourteen reported cases of this condition, states (page 343): "Of the reported cases that I have analyzed in detail, I would exclude on etiologic grounds the cases of Susstrunk, Greenthal and Happ from being true examples of anemias of the new-born of unknown cause. Greenthal's case showed positive evidence of cerebral hemorrhage after high forceps delivery, and Happ's case, a tuberculous mother and an extreme type of asphyxia neonatorum."

In Dr. Abt's analysis of these reported cases (table 2) one notes: grip in the mother during pregnancy, one case; hypertension and toxemia in the mother, one case, and tuberculosis in the mother, one case. These conditions are of too frequent occurrence to play an important rôle in the production of anemia in the new-born infant, particularly when these complicating conditions are not severe.

In the case reported by me (*Arch. Pediat.* **47**:171, 1930), I stated: "The mother, aged 33 years, has had several attacks of pleurisy since girlhood (1909), but has been otherwise well. She was well during pregnancy. . . . When the baby was aged seven weeks, the mother developed another attack of pleurisy with subsequently a pleural effusion, from which she has recovered. . . . She has had no anemia before or after birth of patient." As this mother was clinically well during pregnancy and had previously given birth to a normal child, it seems doubtful that the postpuerperal pleurisy was adequate explanation for the anemia in the infant, although this was offered in my paper as a possible factor. The patient in the case reported responded to treatment, as did those in the other cases reported, and the mother has subsequently enjoyed good health.

It seems doubtful that the same etiologic factor or factors are operative in all these cases. At any rate, the present knowledge would make it questionable to exclude this case on the basis of the maternal history. Asphyxia neonatorum was present, but there was no indication of cerebral hemorrhage. This condition is not productive of anemia. Until further progress is made in etiology, it would seem advisable to include in this group instances of anemia in new-born infants not secondary to sepsis of other infections or to bleeding.

WILLIAM M. HAPP, M.D., Los Angeles.

To the Editor:—In my article entitled "Anemia of the New-Born," which appeared in volume 43, February, 1932, of the AMERICAN JOURNAL OF DISEASES OF CHILDREN, page 337, I attempted to define the essential characteristics of this condition after a careful study of the cases reported in the literature. I stated (p. 337) that "The infants are born of healthy parents, in normal spontaneous labor, and from their history has been excluded all evidence of birth injury, hemorrhage, hemorrhagic disease, infection, or prenatal poisoning." Further on, in an analysis of the cases reported in the literature, I stated (p. 342): "The family history and the health of the parents and of other previously born children were entirely normal, with the exception of the cases reported by Ecklin, Susstrunk,

Greenthal and Happ." Also (p. 342) I said: "The birth histories were normal in all cases except those reported by Foote in 1928 and 1929, Ehrmann, Greenthal, and Happ."

H. H. Donnally, who reported the second case of this group (Anemia in the New-Born, AM. J. DIS. CHILD. **27**:369 [April] 1924), clearly stated that (page 369): "To account for anemia in the early months of life, it is very natural to turn to the mothers of such infants. An explanation may be found in some mothers who have had acute illness while pregnant or who are suffering with tuberculosis or syphilis; in mothers of advanced age and weak constitution; in neuropathic mothers, particularly with enteroptosis and anemia; and in mothers who have had repeated pregnancies at short intervals with abortions and hemorrhages." Speaking of conditions in the infant that might cause such an anemia, Donnally further stated (page 370) that among discoverable causes may be mentioned infection of the young infant with pyogenic organisms, tuberculosis, syphilis, or other infections, as well as traumatic and spontaneous hemorrhages, including the hemorrhagic disease of the new-born. He goes on to say that it is conceivable that the offspring of a mother addicted during her pregnancy to the use of a hemolytic drug such as acetanilid, or of a mother poisoned by mineral poison, benzol or other organic compounds, might be anemic early in life.

While Dr. Happ intimates that maternal causes do not play an important rôle in the production of anemia of the new-born, and while on the part of the infant he would exclude only those anemias secondary to sepsis of other infections or to bleeding, I am more inclined to think that the broader causes of exclusion, so excellently stated by Dr. Donnally, would be preferable in the present state of knowledge.

In studying the case reported by Dr. Happ in the *Archives of Pediatrics* (**47**:171, 1930) I noted (p. 175): "The mother, aged 33 years, has had several attacks of pleurisy since girlhood (1909), but has been otherwise well," and (p. 176): "September 12, 1926, when baby was aged seven weeks, the mother developed another attack of pleurisy with subsequently a pleural effusion, from which she has recovered. A guinea pig inoculated with this pleural fluid, December 28, 1926, was autopsied February 7, 1927, with definitely positive findings for tuberculosis." Obviously, these facts indicate definite evidence of maternal tuberculosis.

As to the condition of the infant at birth Dr. Happ states (p. 175): "The cord was short and around his neck and he was asphyxiated. There were no heart sounds audible; prolonged artificial respiration and intratracheal insufflation were necessary, and ten minims of adrenalin were injected into the heart."

These facts may be interpreted to indicate a decided, if not alarming, asphyxia. Naturally, one would be led to exclude from this group of anemia of the newborn both mother and child because of maternal tuberculosis and prolonged postnatal asphyxia. This was done because I followed the classification of Dr. Donnally, contained in his original report.

I should be willing to include Dr. Happ's reported case in the group that I reviewed if I have in any way misinterpreted the facts in his case report.

ARTHUR F. ABT, M.D., Chicago.

Abstracts from Current Literature

Anatomy and Physiology

THE INFLUENCE OF ULTRAVIOLET LIGHT ON PLASMA CLOT FORMATION. JOHANNES P. M. VOGELAAR and WILLIAM B. WARTMAN, Am. J. M. Sc. **182**:605 (Nov.) 1931.

Bovine blood was citrated and the plasma obtained by centrifugation. This, in turn, was irradiated at room temperature from one to four hours. The plasma was then thoroughly mixed with Ringer's solution and allowed to clot. A control tube containing normal plasma was prepared. As a result the formed clots, demonstrated both macroscopically and microscopically, were increased respectively in tubes irradiated from one to four hours. It is suggested that this is due to an imbibition of water by the fibrinogen as it forms fibrin, resulting in an alteration of the index of refraction.

HENSKE, Omaha.

THE RELATIVE INCREASE IN METABOLISM OF THE LIVER AND OF OTHER TISSUES DURING PROTEIN METABOLISM IN THE RAT. WILLIAM DOCK, Am. J. Physiol. **97**:117 (April) 1931.

The oxygen consumption of rats and rat tissues was compared in two groups of animals, one fed casein and vitamins. The oxygen consumption of the kidneys, in terms of oxygen per minute per hundred square centimeters of body surface, was practically the same in both groups, although the total oxygen intake of the high protein group was 35 per cent greater than that of the low protein controls. The oxygen consumption of the hind quarters was only 8 per cent higher in the rats on a high protein diet, while that of the abdominal viscera was 141 per cent greater during protein feeding. At least 85 per cent of the heat evolved as a result of the specific dynamic action of protein in rats anesthetized with a brand of chlorbutanol-N. N. R. is liberated in the abdominal viscera, probably chiefly in the liver.

KUGELMASS, New York.

THE AZYGOS LOBE OF THE LUNG. E. G. STOLOFF, Am. J. Roentgenol. **22**:466 (Nov.) 1929.

The azygos lobe was visualized in six children. This is significant because the superior mediastinal widenings in children are frequent and demand careful interpretation. The azygos vein may invaginate a fold of pleura during its formation and appear as a fine line with its convexity lateral, coursing from the apex of the lung downward and then inward and medially to approach the mediastinum at about the level of the second costal cartilage. Here it ends as a small dense shadow, which is usually about the size of a pea and may be shaped like a comma, a coffee bean or an elongated diamond.

STULIK, Chicago.

THE SIZE OF THE HEALTHY HEART AND ITS MEASUREMENT. D. EVAN BEDFORD and H. A. TREADGOLD, Lancet **2**:836 (Oct. 17) 1931.

These studies are based on the measurements of 116 orthodiagrams correlated with the body measurements, such as weight, height, circumference of the chest and surface area of the body. The records were from healthy men aged from 18 to 40 years. The total transverse diameter was found to be the most reliable index of the size of the heart for practical purposes. The transverse diameter varies directly with body weight, but not with height. At any given weight, the

transverse diameter varies inversely with height. "Measurements cannot be applied as a rule-of-thumb method in separating healthy from diseased hearts, but must be considered in relation to the clinical data. In border line cases changes in the shape of the heart silhouette, viewed from different angles, are likely to be of more value than measurements."

LANGMANN, New York.

DETERMINATION OF THE SIZE OF THE HEART IN A NORMAL INFANT BY THE TELECARDIOGRAM. OTTO RIEDEL, Arch. hosp. de ninos **2**:11 (March) 1931.

The exact size of the heart in childhood can be obtained only by means of the telecardiogram and orthodiagram. In infancy only teleradioscopy or roentgen examination at short distances can be used. The only diameters of practical value in determining the size of the heart are the transverse diameter and the longitudinal diameter.

SCHLUTZ, Chicago.

THE TRANSFORMATION OF FAT INTO CARBOHYDRATE: I. PHOSPHATIDES AS PRECURSORS OF FAT OXIDATION. HANS JOST, Ztschr. f. physiol. Chem. **197**:90, 1931.

Perfusion experiments on the isolated dog liver were performed with and without the addition of phosphatide. Determinations were made of the partition of phosphatide between blood and liver, the effect of the added phosphatide on the consumption of oxygen and the output of carbon dioxide and the formation of ketones and sugar. Livers containing glycogen but poor in fat were obtained from animals that had fasted one day, while livers rich in fat were obtained by phlorizination for four days during fasting. The phosphatide (lecithin, keratin) added to the perfusion liquid, in contrast to that originally present in the blood corpuscles, is rapidly taken up by the liver. The phosphatide initially present in the fat liver splits off considerable orthophosphoric acid, but in the liver containing glycogen, where the metabolism is less adapted to the utilization of fat, this cleavage of phosphatide could not be clearly demonstrated. In the experiments on livers containing glycogen the addition of phosphatide led to an increase in oxygen consumption and the formation of aceto-acetic acid, while the respiratory quotient fell considerably. In similar experiments with the phlorizinized fat livers the addition of phosphatide altered the steeper curve of ketone formation, but here also the oxygen consumption increased and the respiratory quotient fell. The striking observation, however, is that sugar formation is greatly increased as compared with the control observations without phosphatide. It appears that the breakdown of fatty acids occurs through the intermediary formation of phosphatide. In perfusion experiments with phlorizinized fat liver, sugar is formed from the fatty acid component of the phosphatides.

KUGELMASS, New York.

Pathology, Bacteriology and Biochemistry

THE ORIGIN OF CARIES. GRUNIG, Mitt. Lebensm. Hyg. **22**:52, 1931.

The absence of vitamin B from the diet of guinea-pigs resulted in a discoloring and softening of the enamel of the teeth, probably caused by the quantitative or qualitative change in saliva following the hypotrophy of the salivary glands that was also shown to occur.

KUGELMASS, New York.

THE LEAD CONTENT OF HUMAN BONES. E. BARTH, Virchows Arch. f. path. Anat. **281**:146, 1931.

The bones of ten infants and of thirty adults who had not suffered from lead poisoning were analyzed by P. Schmidt's method, which is described in detail in this paper. In 3 Gm. of bone ash from infants, from 0.01 to 0.04 mg. of lead was found. This quantity is within the limits of error. With an increase in

age larger amounts were found: from 0.02 to 0.19 mg. in 3 Gm. of bone ash. There was no difference in lead content between the bones of people from a rural community without a central water supply and those of persons from the city. The lead was found in the compact part of the bone. The author thinks that it is chiefly taken in with food containing traces of lead.

SCHOENTHAL, New York.

EXAMINATION OF THE PERMEABILITY OF THE HUMAN PLACENTA FOR DEXTROSE. H. RUNGE and H. HARTMANN, Ztschr. f. Geburtsh. u. Gynäk. **98**:290, 1930.

This is a short confirmation of a previous article published in the same journal (*Ztschr. f. Geburtsh. u. Gynäk.* **96**:324, 1929).

ADAIR, Chicago.

THE INFLUENCE OF THE FEMALE SEX HORMONE IN THE JUVENILE MALE GENERATIVE GLANDS. PAUL GERÉB, Ztschr. f. Geburtsh. u. Gynäk. **99**:443, 1931.

The author injected the urine of pregnant women into immature male mice. In a second group of investigations, the anterior pituitary hormone was first extracted from the urine of pregnant women, so that it contained only the female sex hormone. It was found that premature spermatogenesis is developed not only by the anterior pituitary hormone but by the female sex hormone. The female sex hormone has first a stimulating effect on the male generative gland and later a retarding effect.

ADAIR, Chicago.

AGE VARIATIONS IN THE SENSITIZATION PHENOMENON IN EXCISED VESSELS. S. MORISHIGE, J. Pediat. (Tokyo), Sept. 20, 1931, no. 376, p. 1305.

The author used arteries from the ears of rabbits during various age periods, and prepared them for experimental sensitization with diluted horse serum, first washing out the blood by means of a Ringer-Locke solution and then allowing them to remain in the refrigerator for twenty-four hours. A similar method was employed with the distal portion of the aorta in guinea-pigs. The experimental animals were all given an initial injection of horse serum previous to the excision of the vessels. The degree of contraction of the vessels with the perfusion of dilute horse serum was measured in terms of the number of drops of perfused solution collected on a glass plate. In adult animals the degree of contraction was far greater than in the young, and the duration of this reaction also was greater. In passive sensitization, however, there seemed to be no appreciable difference according to age period. This fact is explained by the author as being due to inadequate antibody formation in the young.

KATO, Chicago.

Nutrition

THE EFFECT OF INTRAVENOUS AND INTRAPERITONEAL INJECTIONS OF IRRADIATED ERGOSTEROL. C. I. REED and E. A. THACKER, Am. J. Physiol. **96**:21 (Jan. 1) 1931.

Viosterol in corn oil (10 mg. per cubic centimeter) was administered intravenously or intraperitoneally in repeated varying doses to fourteen dogs. The effect was greater than with comparable doses by mouth. The toxic effect of large doses was greater by these methods, due probably to the reduction of the ergosterol to coprosterin in the intestinal tract.

The experiments indicated the following additional points: Toxic symptoms do not necessarily parallel the hypercalcemia; a certain degree of tolerance may develop after continued administration of therapeutic doses, as shown by a reduction in the hypercalcemia; hypercalcemia may persist for long periods after administra-

tion has been discontinued; when pronounced toxic symptoms developed, none of the animals in the series recovered after discontinuance; there was no constant effect on the concentration of inorganic phosphorus in the blood; microscopic examinations of tissues revealed deposits of calcium only in the kidneys, and the only evidence of tissue injury was found in a rather uniform degeneration of the kidney tubule epithelium.

NOURSE, Cleveland.

SOFT-CURD MILK: NATURE'S FOOD FOR INFANTS. REUBEN L. HILL, Arch. Pediat. **48**:417 (July) 1931.

"The term soft-curd milk, now in scientific literature, originated with the author to describe milk on which coagulation with the pepsin or rennin ferment forms a coagulum that is soft and clabbery in consistency, differing widely from the tough rubber-like curd obtained from most samples of cows' milk."

The Hill test for determining the consistency of the curd of various milks is described, and the wide range of variation of curd is discussed. The author finds the curd tension to vary from 12 Gm. to 250 Gm.

"When soft-curd milk is available, the feeding problem becomes much simpler. Experimental results would indicate that this milk is easily digested without dilution or modification, and that it can be used in a concentrated form. Since there is no dilution, the normal sugar content of milk is sufficiently high not to require the customary sugar supplementation. The addition of lactic acid to produce an acid curd apparently is not necessary when soft-curd milk is used. It thus seems possible to supply milk that is sweet and has a normal reaction and has not been abnormally sweetened by the addition of sugar, nor made acid by the use of lactic or citric acid, nor made alkaline by the use of lime water or soda. The use of a normal milk is obviously superior to milk that is either abnormally acid or alkaline in reaction. Researches at this station to date indicate a superiority of hard-curd milk over soft-curd milk for the manufacture of cheese. This may ultimately free soft-curd cows for market milk dairies."

WADDELL, University, Va.

A CRITICAL CLINICAL STUDY OF CONCENTRATED AND DRIED INFANT FOODS. ADOLPH G. DE SANCTIS and JOHN DORSEY CRAIG, Arch. Pediat. **48**:439 (July) 1931.

This article is the first in a series of articles in which the authors plan to examine clinically the merits of different infant foods.

It is pointed out that no scientifically controlled work has been done on sweetened condensed milk. The authors record their findings in the cases of fifty infants fed condensed milk, and compare their results with a control series of fifty cases in which milk, water and added carbohydrates were given:

"The results of a critical clinical study of fifty infants fed sweetened condensed milk are reported. It is shown that sweetened condensed milk apparently meets the nutritional requirements of the normal infant. We have found that the dilutions of condensed milk ordinarily and commonly used are too strong for the average infant. Vitamins A and B are both present in sufficient quantity, and vitamins C and D must necessarily be supplied by anti-scorbutic and antirachitic agents. Condensed milk is easily digested by the normal infant.

"It has been definitely shown that the number of bacteria in this food is not sufficient to affect or injure the health; that no pathogens are present.

"The gain in weight and the physical development in general in our series of cases compare favorably with groups fed various foods.

"Secondary anemia does not result directly from the feeding of condensed milk. There was no greater incidence of secondary infection in this group of cases than in a control group. With the administration of a sufficient amount of antiscorbutic agent no manifestation of scurvy occurred. The incidence of rickets is not any higher than in infants fed other foods."

WADDELL, University, Va.

RAW BASIC FEEDING IN ANOREXIA OF CHILDHOOD. I. NEWTON KUGELMASS and EMMA L. SAMUEL, Arch. Pediat. **48**:457 (July) 1931.

The authors discuss briefly some of the causes of anorexia and the mechanism of the various digestive stages. They suggest a raw basic diet in the early treatment for anorexia, and state that appetite can be stimulated by meals of this type. Foods chosen for the anorexia diet are those which may be eaten raw, in season, such as sound, ripe well washed fruit and crisp, clean, chilled vegetables. Attention is called to the attractive serving of such foods. The total effect is one of more complete emptying of the alimentary tract, thus favoring the development of more marked hunger contraction and its stimulation of the so-called hunger period.

WADDELL, University, Va.

THE MAL-TREATED CAUSE OF MALNUTRITION. EMILY P. BACON, Arch. Pediat. **48**:471 (July) 1931.

This article suggests nothing new, and is simply a restatement of things said many times before. A better title would have been "The Causes and Treatment of Anorexia."

WADDELL, University, Va.

THE EFFECT OF LARGE DOSES OF IRRADIATED ERGOSTEROL UPON THE ASH CONTENT OF THE FEMORA OF YOUNG AND ADULT RATS. JAMES H. JONES and GEORGE M. ROBSON, J. Biol. Chem. **91**:43 (April) 1931.

Contrary to the conclusions of several other investigators, these authors report that toxic doses of irradiated ergosterol have but a slight effect in reducing the percentage of ash in the bones of either adult or growing rats, as determined by ash analyses of the femora. In growing rats the relative amount of ash may be slightly decreased, but there is no detectable decrease in the absolute amount. It is argued that the absolute amount of ash in the bone, rather than its relative amount, should be considered in determining withdrawal of ash from bone. The pathologic changes in the heart, aorta, kidneys, gastro-intestinal tract, lungs, spleen and liver of rats given toxic doses are recorded.

BUTLER, Boston.

DIETARY REQUIREMENTS FOR FERTILITY IN LACTATION: XXIII. THE SPECIFIC EFFECT OF VITAMIN B ON LACTATION. BARNETT SURE and DOROTHY J. WALKER, J. Biol. Chem. **91**:69 (April) 1931.

Earlier work of these authors presented evidence that lactating rats given diets deficient in vitamin B consumed less food than similar rats receiving the same diet but fortified with an abundance of this vitamin. This paper presents data showing that vitamin B not only affects the amount of food ingested but also exerts a specific effect on lactation, as characterized by growth and survival of the nursing young. This effect is independent of water and food intake.

BUTLER, Boston.

COMPOSITION OF BONE: X. MECHANISM OF HEALING IN LOW PHOSPHORUS RICKETS. B. KRAMER, M. J. SHEAR and J. SIEGEL, J. Biol. Chem. **91**:271 (April) 1931.

The preliminary experiments reported in this paper show that roentgen examination before autopsy is not as delicate a method for the detection of small amounts of newly deposited bone as histologic examination. Therefore, in pooling the blood of rats for chemical examination during the process of healing active rickets, blood was collected separately from each animal and pooled for analysis only after histologic examination had been made. The serums from rats showing similar histologic pictures were thus combined. Rickets was produced in rats in the usual manner on Steenbock and Black ration no. 2965. Whether the healing was induced by cod liver oil, irradiated ergosterol, phosphate, fasting or irradiation,

the serum calcium × phosphate product preceding of the resumption of calcification was not resumed when the calcium × phosphorus product was below 40. It always ceased when the product was below 30. Healing induced by cod liver oil or irradiated ergosterol was noted histologically by the third day; that induced by fasting was noted within twenty-four hours, and that induced by added phosphate was noted within twelve hours. In the healing caused by added phosphate the rise in serum phosphate was accompanied by a fall in serum calcium. This fall was sufficient to cause the appearance of signs of tetany. The administration of cod liver oil did not prevent this early sudden drop in the serum calcium. Rickets produced on the diet of Hess, Weinstock, Rivkin and Gross was, contrary to that reported by these authors, accompanied by a low calcium × phosphorus product. When calcium was added to this diet the product was still below 30. The authors feel that the precipitation theory of calcification offers the best explanation of the observations presented in this paper.

BUTLER, Boston.

THE MINERAL, NITROGEN AND FAT CONTENT OF SOME VARIETIES OF MATURE BEAN SEED AND OF STRING BEANS. J. S. McHARGUE and W. R. ROY, J. Nutrition **3**:479 (March) 1931.

Eleven varieties of beans were analyzed. The results showed a high and rather uniform mineral content. The nitrogen content was high, and the results for copper, manganese, zinc and iron showed that the varieties analyzed are fairly well supplied with these metals.

The authors believe that the curative property of beans for beriberi is associated with their relatively high mineral content.

MUNNS, Winnetka, Ill.

VITAMINE STUDIES: XVIII. THE BIOLOGICAL ASSAY OF FOOD MATERIALS FOR VITAMINE A AS INFLUENCED BY YEAST FROM VARIOUS SOURCES. H. E. HONEYWELL, R. A. DUTCHER and J. O. ELY, J. Nutrition **3**:491 (March) 1931.

A biologic assay of food materials for vitamin A was performed after the method suggested by Sherman and Munsell. About 700 rats were used in conducting the experiment. Two drops of butter fat daily were used as a constant and uniform source of vitamin A. The authors found that yeasts made by the same manufacturer may or may not contain traces of vitamin A, and that the vitamin A response when the curative method is used will vary, depending on the yeast used as a source of the vitamin B complex. They also observed that vitamin A may consist of two factors, one possessing antiophthalmic properties and tending to preserve the normality of other epithelial tissues, and the other factor possessing the growth-stimulating properties usually ascribed to vitamin A.

MUNNS, Winnetka, Ill.

OBSERVATIONS ON THE ASSAY OF THE ANTINEURITIC VITAMIN. W. H. SEBRELL, Pub. Health Rep. **46**:917 (April 17) 1931.

The symptoms of polyneuritis in rats appear to be associated with a shortage rather than a complete absence of the antineuritic vitamin. The curative method for testing antineuritic concentrates on rats may be applied by injecting a suitable solution of the concentrate subcutaneously or intraperitoneally.

SANFORD, Chicago.

REPORT OF COMMITTEE ON MILK. E. G. BROWN, Pub. Health Rep. **46**:1455 (June 19) 1931.

The Committee on Milk warns against reduction of the amount of milk allowed children for economic reasons. It should be increased rather than decreased. They also call attention to two papers recently published by Scott and Erf and

by Mattich and Golding on rats, in which it was stated that raw milk possesses a significant dietary superiority over pasteurized milk. In a number of states reprints are being prepared of this material and distributed broadcast by the raw milk dealers in an effort to discredit pasteurized milk in the mind of the consumer. The Committee gives abstracts from papers by Oyster, Brannon, Lane-Claypon and Leighton and McKinley, in which similar observations were made on babies, with no significant difference shown. More work is being carried out on this by the public health organization. "After all, what we are interested in is the effect of milk upon human babies rather than the effect of milk upon the young animal."

SANFORD, Chicago.

A CLINICAL STUDY OF NUTRITIONAL XEROPHTHALMIA AND NIGHT-BLINDNESS. J. C. SPENCE, Arch. Dis. Childhood **6**:17 (Feb.) 1931.

In one year 11 cases of nutritional night-blindness were found among a total of 4,100 patients visiting the ophthalmologic department of a clinic in northern England. Nine of these patients were under 13 years of age. There was a history of deficient diet in all cases, very little or no animal fat or protein having been eaten. The most characteristic sign of the disease is Bitot's spots, which are opaque whitish deposits on the scleral conjunctiva. The disease was found in children whose general condition and rate of growth had been well maintained. There was no evidence of rickets or other deficiency diseases in the affected patients.

A maximum rate of cure was studied by adding large amounts of cod liver oil, butter and milk. Using this as a basis, it was shown that viosterol, ultraviolet irradiation and liver extract have no effect on xerophthalmia.

In the active stage of the disease large amounts of epithelial cells were found in the urine. This is a clinical confirmation of Wolbach and Howe's discovery that vitamin A deficiency results in damage to epithelial structures.

KELLY, Milwaukee.

THE HYDROGEN ION CONCENTRATION AND THE CALCIUM AND PHOSPHORUS CONTENT OF THE FECES OF RACHITIC CHILDREN. THURZA REDMAN, Biochem. J. **23**:256, 1929.

The p_H, calcium and phosphorus contents of the stools of a group of rachitic children kept on a controlled diet with various therapeutic measures were studied. A degree of correlation exists between the p_H and the calcium and phosphorus. The best clinical results were obtained in the group treated with irradiated cholesterol, and in this group the feces were constantly acid. Healing occurs more rapidly when the phosphorus is consistently low.

BOYD, Toronto, Canada.

THE INFLUENCE OF DIET ON CARIES IN CHILDREN'S TEETH. COMMITTEE ON DENTAL DISEASE, MEDICAL RESEARCH COUNCIL, report 159, 1931.

This report deals with the effect of fat-soluble vitamins on the progress of caries. In two groups of children numbering from sixty-five to eighty-six, living under similar conditions and having a standard diet for two years, the group receiving and added ration of fat-soluble vitamins had only one-third the increase of caries that was found in the other group to whose diet olive oil and treacle were added. There was no significant difference in the rate of increase of caries between the children receiving olive oil and those receiving treacle.

In another two groups of eighty-two and seventy-nine, respectively, under the same conditions, one group received an addition of olive oil, and the other olive oil to which a solution of vitamin D was added. Over a period of one year and a half, the progress of caries in the permanent teeth was also significantly retarded in the vitamin group.

SANFORD, Chicago.

TREATMENT FOR CHOLERA INFANTUM. A. B. MARFAN, Nourrisson **19**:40 (Jan.) 1931.

Omission of all foods and the administration of water by mouth are advised for the first two or three days in cholera infantum. The absorption of water from the gastro-intestinal tract is more reliable and effective than that introduced by the various other routes so frequently used. If some improvement is not noted in two or three days on the water-diet, the prognosis is poor. Following starvation, breast milk, if obtainable, should be begun in small amounts. If this is lacking, buttermilk is the second choice. Increases are made slowly according to the condition of the patient. Subcutaneous injections of saline or dextrose have not been found helpful. The cardiac stimulants recommended are camphor and caffeine. Hot baths are also helpful.

Subcutaneous, intravenous and intraperitoneal injections of the commonly used isotonic solutions are discussed but not recommended. Blood transfusions, both intravenous and intraperitoneal, are considered to be still in the experimental stage, and final decision regarding their worth must be left to the future. The employment of intramuscular injections of insulin combined with subcutaneous injections of dextrose is mentioned, but benefit has not as yet been proved. The value of lavage of the stomach and intestine is also doubted.

McCLELLAND, Cleveland.

THE BEHAVIOR OF THE p_H IN THE MILK OF A WOMAN SUBJECTED TO IRRADIATION WITH ULTRAVIOLET RAYS AND TO THE INHALATION OF IRRADIATED AIR. A. FIORENTI, Riv. di clin. pediat. **29**:273, 1931.

Ultraviolet irradiation was applied to the region of the breasts of eleven nursing mothers for from ten to fifteen minutes. Eleven other nursing mothers breathed irradiated air for twenty minutes. The milk at first became more acid, but after two or three hours it usually became more alkaline than before the irradiation. A greater effect was noticed when irradiated air was breathed.

HIGGINS, Boston.

DEHYDRATION IN INFANCY. P. LETONDAL, Arch. méd.-chir. hosp. Ste. Justine, Montreal, 1931.

The author has used Hartmann's solution in twenty-two cases of dehydration with only a 22.7 per cent mortality, and considers this to be the fluid of choice. It may be given intraperitoneally, subcutaneously, orally or rectally.

SANFORD, Chicago.

CONDENSED MILK IN THE TREATMENT OF VOMITING IN THE INFANT. J. P. GARRAHAN and C. M. PINTOS, Rev. de especialid. **5**:1671 (Nov.) 1930.

A child, 6 months old, weighing 3,650 Gm., continued vomiting on several different foods. The authors finally used condensed milk, and the child's weight rose to 4,700 Gm. in one month.

SANFORD, Chicago.

DIAGNOSIS OF VITAMIN A DEFICIENCY (KERATOMALACIA) BY BACTERIOSCOPY OF THE CONJUNCTIVA. ARNOLD PILLAT, Ztschr. f. Augenh. **73**:244 (Feb.) 1931.

A case history is given of a child, 2 months old, who showed a clinical picture of keratomalacia in the left eye and an apparently normal right eye. The examination of the corneal tissue revealed a like bacterial flora in both eyes, notwithstanding the normal appearance of the right. Pillat asserts that it is possible to detect early stages of keratomalacia by the superabundance of the saprophytic organisms, particularly the xerosis bacillus in the epithelium of the cornea. He observed that when the cornea of a normal eye is scraped in the usual manner with a platinum loop, few or no cells are rubbed off, whereas in keratomalacia the

cells are plentiful in the scraping. The epithelial cells are distorted and stain poorly. There are very few lymphocytes or leukocytes in the scrapings. The author believes that the damage to the eye is produced primarily by a degenerative process and not by an inflammation and that the proliferation of the germinal layer is not increased by irritation but by the proliferation of the saprophytes on the degenerative tissue. This picture of keratomalacia is in accord with that published by the abstractor in the *Archives of Ophthalmology* (**52**:416 [Sept.] 1924).

YUDKIN, New Haven, Conn.

A CASE OF ENDOGENOUS PERENNIAL RICKETS RESISTANT TO VITAMIN D AND LIGHT. P. BORNSCHEUER, Ztschr. f. Kinderh. **51**:56 (May) 1931.

A case of rickets is reported in a girl who had been treated up to the age of 2¼ years by a local physician. At 7 years she was operated on for bow legs. At the age of 12 years and 7 months she was admitted because she had fallen, and complained of pains in the left side of the chest. She presented, in roentgenograms and chemical blood tests, the picture of florid rickets. Boyd reported a series of cases of diabetes mellitus or insipidus and a disturbed acid-base metabolism, in fact, an acidosis, not amenable to vitamin D therapy. While he caused improvement by the giving of 3 Gm. of sodium bicarbonate daily, Bornscheuer saw the acidosis disappear and the rickets improve with the use of a diet that had a high excess of alkali. There was no change in the composition or excretion of the urine. In the study of the metabolism the calcium retention was high and the retention of phosphorus distinctly increased, the former more than the latter. The pains in the chest and knees went away, and no new fractures of the ribs occurred; the hands showed a zone of calcification, and the child began to grow. No benefit had resulted from sun baths given for five weeks or viosterol given for one and a half months.

EMERSON, Boston.

STOOLS OF THE ARTIFICIALLY FED BABY IN AN INSTITUTION. J. M. JAHR, Ztschr. f. Kinderh. **51**:135 (June) 1931.

The regular changes to be observed in the stools of the artificially fed baby in an institution, which Jahr calls institutional diarrhea, are associated with a definite age, primarily the first three months, independently of the kind of food given. Seventy per cent of the cases progress to an acute disturbance of nutrition. The disease cannot be fully explained on the ground of parenteral infections; it is rather due, as clinical, roentgen and metabolic studies show, to a disturbance of synergy (Freudenburg) of the intestinal functions. Motor and sensory functions, servants of digestion, strike sympathetically. Direct results are the decisive changes in the water economy, in which the relation between the amounts of water excreted by the intestine and kidney is reversed. The utilization of fat is lacking to the extent of from 60 to 90 per cent. Institutional diarrhea is avoidable by minute and individual attention on the part of nurses. Individual nurses, assigned to not more than two babies each, exclude the institutional milieu; special nurses, the same ones always for the same babies, exclude the hospital milieu. By means of both, a diarrhea that has begun is quickly healed without any change in the nutritional regimen.

EMERSON, Boston.

PROPHYLAXIS OF RICKETS. J. H. G. CARSTENS, Nederl. tijdschr. v. geneesk. **75**:3550 (July 4) 1931.

The author sought the answer to three questions: For which children is a preventive treatment against rickets necessary? Which preventive treatment is the most desirable? At what age and during what time must the treatment take place?

Five groups of healthy babies, numbering 150, were studied. The children of four groups were protected against rickets in different ways. In the fifth group no treatment was given. At the beginning of the treatment, which lasted from

November till April, the age varied from 6 to 9 months. During April all children who had remained under control were thoroughly reexamined for symptoms of rickets. The conclusions of the author are: Nearly all babies in Holland that are more than 3 months old need preventive treatment against rickets during the winter. Ultraviolet irradiation and different vitamin D preparations are all suitable. The doses of the preparations that the author used are given, and some social and medical consequences of this investigation described.

VAN CREVELD, Amsterdam, Holland.

THE OCCURRENCE OF FAT-SOLUBLE VITAMINS IN DIFFERENT VARIETIES OF FISH, E. POULSSON, Norsk mag. f. lægevidensk. **92**:125 (Feb.) 1931.

The author first discusses the technic of determining the amounts of vitamins A and D contained in different varieties of fish. During recent years there has been competition between the cod liver oil from Norway and that from Newfoundland. It has been stated that the cod liver oil from Newfoundland contains from twelve to twenty-one times the antirachitic vitamins contained in the oil from Norway. According to investigations performed at the State Vitamin Institute of Norway during 1929 on fifty-eight different specimens of Norwegian cod liver oil, this is not the case. The least effective dose of Norwegian cod liver oil as far as the antirachitic effect is concerned was found to be from 4 to 5 mg. In a few instances 6 mg. was required, but sometimes 3 mg. was sufficient. In the case of thirty-nine specimens of cod liver oil from Newfoundland a double dose had to be used. The author believes that the explanation probably must be sought in the fact that the Norwegian cod liver oil comes from spawning fish while the American oil comes from fish caught a long time after the spawning season.

The cod is far from being the only fish that gives a highly antirachitic liver oil. The fact that the liver oil of the cod is always used in medicine is mostly because the cod is a very common fish that returns every year to certain places, so that it forms a good source of material. Lota vulgaris, which lives in lakes and belongs to the cod family, has a vitamin content eight times that of the cod. Shark livers contain usually much more vitamin A than do those of the cod, whereas vitamin D is contained in just a small amount, about one tenth of that in the cod. In sharks growth proceeds rapidly, which may be the explanation of the high vitamin A content. Sharks are cartilage fish which show very little calcification of the skeleton, and they do not have much need of vitamin D, which is essentially a calcification vitamin.

The author closes his article with the well known sentence of the Swiss writer: "Die Natur ist doch ein wunderbarer Künstler."

TOVERUD, Oslo Norway.

Prenatal Conditions

CONGENITAL MALFORMATIONS OF THE INTESTINAL TRACT AND BILE DUCTS IN INFANCY AND IN CHILDHOOD. WARREN H. COLE, Arch. Surg. **23**:820 (Nov.) 1931.

The author has analyzed all cases of congenital malformation of the intestine and bile ducts that occurred in a series of 45,000 admissions to the St. Louis Children's Hospital during the past fifteen years. All cases of hypertrophic pyloric stenosis, of which there were 81, were omitted in the discussion. In this large number of hospital patients there were only 81 instances of congenital malformation of the intestines. These included malformation of practically every part of the intestine. Hirschsprung's disease occurred in 11 children, while imperforate anus was noted in 8 infants. The other malformations were less common. The etiology, diagnosis and treatment are well discussed in this series, which stresses the importance of always considering a congenital malformation when unusual symptoms manifest themselves within the first few months of life.

KAISER, Rochester, N. Y.

BILATERAL SYMMETRICAL INTRA-UTERINE FRACTURES OF THE FEMUR; BILATERAL EQUINOVARUS CLUBFOOT. C. ROEDERER, Bull. Soc. de pédiat. de Paris **29**:69 (Feb.) 1931.

A boy, first seen when 2 weeks old, had marked deformity of both thighs due to subtrochanteric fractures of the femora. The deformity was noted at birth by the obstetrician, and as no unusual force was employed the bilateral fractures must have occurred in utero. At 6 months of age the fragments of the bones were united in poor alinement, and roentgenologic examination showed irregular calcification with areas of density and of rarefaction. The other bones were normal.

BENJAMIN, Montreal, Canada.

A CASE OF PERIOSTEAL DYSPLASIA. C. ROEDERER, Bull. Soc. de pédiat. de Paris **29**:71 (Feb.) 1931.

A case previously presented by the author as showing bilateral symmetrical intra-uterine fracture of the femur was thought to be due to periosteal dysplasia by a colleague. Periosteal dysplasia is hereditary, is seen in the middle of the diaphysis and usually appears somewhat later in life. A boy, 9 months old, showed bilateral fractures of the long bones at the middle of the shafts with marked callus formation even where the line of fracture could hardly be discerned. Roederer believes this to be a case of periosteal dysplasia.

BENJAMIN, Montreal, Canada.

VICTOR CATHALA'S REPORT ON "HEREDITY OF AN ACQUIRED MUTILATION." GEORGES SCHREIBER, Bull. Soc. de pédiat. de Paris **29**:90 (Feb.) 1931.

Cathala reported that a mother who, at the age of 3 years, had had two fingers of the left hand amputated as a result of trauma, gave birth to a baby who showed a similar congenital malformation. Schreiber is not satisfied that the mother's deformity was acquired, and believes that it may have been congenital, and that the infant's malformation was a reproduction of a congenital malformation, as frequently occurs, and not of an acquired one, which occurs extremely rarely if at all.

BENJAMIN, Montreal, Canada.

CONGENITAL MALFORMATIONS OF THE SPINE (ANTERIOR RACHISCHISIS). E. SORREL and LEGRAND-LAMBLING, Bull. Soc. de pédiat. de Paris **29**:94 (Feb.) 1931.

The authors present two cases illustrating congenital deformity of the spine. When there is simply an anterior rachischisis a kyphosis is present which is sometimes erroneously thought to be due to Pott's disease. When other spinal abnormalities accompany the rachischisis, scoliosis is usually present. In certain instances there may be considerable congenital malformation of the spine without any visible deformity; one such case is mentioned. Here the spinal abnormalities are discovered only by means of the roentgenogram.

BENJAMIN, Montreal, Canada.

FETAL PERITONITIS DUE TO BACILLUS FECALIS-ALCALIGENES. H. SLOBOZIANA and M. NASTA, Compt. rend. Soc. de biol. **107**:851 (June 30) 1931.

A rare infection is described. Twins born at full term, weighing 3,000 and 2,400 Gm., respectively, showed signs of peritonitis. The mother was well during the pregnancy. One baby died in thirty-six hours and the other in five days. At autopsy in each case a fibropurulent exudate was found in the abdomen. In one case, atresia of the ileum, a microcolon and infarction of the lung and pancreas were present. No enteritis was found. The organism was identified as a motile

gram-negative bacillus showing abundant growth on gelatin. It was a dirty gray and viscid, but did not liquefy the medium. It showed a tendency to form a film on broth; indol was produced in a peptone medium. The organism did not ferment mannite, maltose, saccharose, lactose, galactose or arabinose. There was no agglutination with the serum of persons with typhoid or paratyphoid A, B or C. These characteristics permitted the identification of Bacillus fecalis-alcaligenes in the cases described.

WAHL, Cleveland.

PERSISTENT URACHUS WITH VESICO-UMBILICAL FISTULA AND LITHIASIS. OTA SLOVAČEK, Časop. lék. česk. **68**:1335 (Sept. 27) 1929.

The diagnosis of persistent urachus was made in a man aged 35. At operation he was found to have urate stones, which were a source of colic. Complete extirpation was followed by complete cure. This is apparently the first time a coincident lithiasis in a case of persistent urachus has been described.

STULIK, Chicago.

DICEPHALUS. KAREL HORA, Časop. lék. česk. **68**:1406 (Oct. 11) 1929.

The author presents a photograph and roentgenogram of a dicephalus that was born spontaneously. The two heads were well formed, and the spine was bifurcated at the ninth dorsal vertebra; a double spinal column occurred above that point. The anatomic diagnosis is dicephalus tribrachius occultus.

STULIK, Chicago.

Acute Infections

IMMUNITY IN VIRUS DISEASES. W. LLOYD AYCOCK, J. A. M. A. **97**:1199 (Oct. 24) 1931.

The development of immunity to certain infectious diseases in normal persons similar to immunity following an attack of the disease has been thought due to subclinical infection with the disease virus. Others believe that adult immunity arises spontaneously with an increase in age and is not antigenic in origin. It is of epidemiologic importance to know whether adult immunity is antigenic or a maturation phenomenon. The author reviews the cogent data on the subject. He believes that adult immunity, whether accompanied by recognizable manifestations of the disease or not, is a specific immunity and not a maturation phenomenon. Reexposure to the disease is probably an important factor in the maintenance of adult immunity.

BONAR, Salt Lake City.

THE FILTERABILITY OF VACCINIA VIRUS. A. B. GREEN and G. H. EAGLES, Brit. J. Exper. Path. **12**:202, 1931.

The authors claim that vaccinia virus passes readily through Berkefeld V filters and to some extent through Berkefeld N and English Berkefeld filters. The p_H of the virus suspension (6.4-8.4) does not influence the results, and lining the filters with acidified egg white or the use of hormone broth as a diluent is not necessary. These filtrates can be kept in the cold for a week or more without marked deterioration in activity.

C. E. CLIFTON [ARCH. PATH.].

THE CLINICAL AND EPIDEMIOLOGICAL CHARACTERISTICS OF VARIOLA MINOR AND ITS DIFFERENTIAL DIAGNOSIS. CHRIS J. MCSWEENEY, Quart. J. Med. **24**:487 (July) 1931.

The author discusses various aspects of the type of smallpox that has been prevalent in England and Wales for the past eight years. He thinks that the names, "alastrim," "modern smallpox" and "varioloid," are not accurate. A rather

complete clinical picture of "variola minor," as he would designate the disease, is given. A significant feature of the disease is its low communicability rate even in a poorly vaccinated portion of the population. Somewhat influenced by reports concerning postvaccinal encephalitis and by the negligible mortality in this type of smallpox, the author thinks that vaccination as a means of prophylaxis should be used with discretion. He makes the following surprising statement: "Even when the non-classical type of the disease has assumed epidemic proportions in a community, it is doubtful whether the enforcement of generalized vaccination is ever justifiable." He believes that the control of variola minor depends on, first, the accurate and prompt diagnosis of the case and the speedy removal of the patient to the hospital, and second, careful isolation of contacts for a period of three weeks.

BRADFORD, Rochester, N. Y.

THE INFLUENCE OF DOSES OF DIPHTHERIA ANTITOXIN IN ACTIVE IMMUNIZATION OF THE HUMAN BEING. G. RAMON, ROBERT DEBRÉ, M. MOZER and G. MOZER, Compt. rend. Soc. de biol. **107**:485 (June 5) 1931.

The usual method of immunization against diphtheria, by weekly injections of 0.5, 1.0 and 1.5 cc. of antitoxin having a titer of 10 units, gives a negative Schick reaction in 95 per cent of the cases. Ramon and his collaborators increased the antitoxic power to 16 units per cubic centimeter, and injected 1.0, 1.0 and 2.0 cc. at three week intervals into two series of children giving a positive Schick reaction: 123 between 14 and 15 months of age and 142 between 2 and 5 years of age. The first group gave 100 per cent negative Schick reactions in from four to eight weeks following the last injection; the second group, in fifteen days. By this method the antitoxin titer of the serum was elevated to more than one-thirtieth unit. The latter figure represents the serum titer that is necessary for the production of immunity. No mention is made of any reactions.

WAHL, Cleveland.

DIPHTHERIA OF THE SKIN. H. STUX, Nourrisson **19**:228 (July) 1931.

A review of the literature shows that cutaneous diphtheria occurs most frequently in infants aged 2 years and under. In the nursery at Odessa, where normal infants up to the age of 1 year are admitted, sixteen cases of primary diphtheria of the skin were encountered in five years; eight others in which the skin infection was secondary to other diphtheria infection were also seen. Most of the cases occurred during the winter months. Infantile eczema seemed to be a predisposing cause. The course of the disease is usually benign. The cases responded promptly to treatment with antitoxin. In institutions prophylactic measures are important.

MCCLELLAND, Cleveland.

DIPHTHERIA IN URUGUAY. M. RUBINO, J. LEUNDA and J. MOREAU, Paris méd. **1**:447 (May 9) 1931.

The authors studied the 1928 epidemic of diphtheria in Uruguay, and found that in these cases Loeffler's bacillus was much more toxic than usual. Clinically the cases were characterized by extreme toxicity with poor results from serum. The authors thought that the morphologic type of the bacilli might have a bearing on these cases, as the majority were of medium length. (They separate them into short, medium and long groups.)

SANFORD, Chicago.

SERUM THERAPY IN DIPHTHERIA. D. ROUX, Progrès méd., March 28, 1931, p. 569.

In the issue of *Progrès médicale* of Dec. 13, 1930, J. Minet published an article on antidiphtheritic therapy, in which he stated that at present the French antidiphtheritic serum is inferior to the Belgian. Dr. Roux takes exception to this

reflection on the Pasteur Institute and replies with statistics on their antitoxin for the last thirty years. From 1900 to 1902, the mortality in the patients treated was 9.46 per cent. In 1930 it was 1.13 per cent. It has dropped every year since the beginning of its manufacture, owing to improvements in technic. These figures do not indicate that the French serum is inferior.

SANFORD, Chicago.

THE NECROTIC ANGINAS OF SCARLET FEVER AND THEIR TREATMENT WITH ANTIGANGRENOUS SERUM. A. STROE, D. HORTOPAN and J. BAZGAN, Rev. franç. de pédiat. **7**:23, 1931.

This report comes from Bucharest, where there are about 1,500 cases of scarlet fever annually with an incidence of from 2 to 7 per cent of the necrotic anginal type. It is in this type of case with severe toxic symptoms that the authors have used a polyvalent antigangrenous serum which was developed during the war for the treatment of gas gangrene. In 71 cases there were 9 deaths; 39 of the cases were of the severe form, in which the mortality is usually considered to be about 80 per cent. The serum was given in large doses, often 100 cc. a day. The action of the serum is thought to be specific only in the case of *Bacillus perfringens*. This organism was isolated from many of the throats, and serum antiperfringens makes up 40 per cent of the antigangrenous serum. Through further identification the authors hope to develop a more specific serum.

LESLIE, Evanston, Ill.

MALIGNANT DIPHTHERIA. A. GISMONDI, Prat. pediat. **9**:83 (March) 1931.

This article is a good review of the subject but, unfortunately, the bibliography does not include specific references to the works of many of the authors whose names are mentioned in the text. Gismondi's quoted statistics give the impression that both the incidence and the mortality of malignant diphtheria are increasing and that antitoxin is apparently less effectual in combating it. The classic picture of malignant diphtheria is described in detail. Many authors ascribe the increased severity and antitoxin-resisting character of this type of infection to a possible symbiosis with other micro-organisms, particularly the streptococcus. Gismondi disagrees with this view because erysipelas, scarlet fever and other streptococcal diseases do not seem to impart a special gravity to diphtheria when they accompany it, and because there is no correlation between the presence of streptococci in throat cultures and the severity of the diphtheria present. He also depreciates the hypothesis that antitoxin is less efficacious than it was formerly. Mortality statistics indicate that in diphtheria the percentage of deaths due to laryngeal infection is decreasing while the percentage due to angina is increasing. In its pathology, the malignant case corresponds in every detail with the case in which the patient is untreated or insufficiently treated, except that the course of the latter is longer. Therefore, the increasingly prevalent practice of giving very large doses of antitoxin (from 400,000 to 500,000 units) seems the treatment of choice. A combination of intravenous and intramuscular injection is best. Additional treatment may include intravenous injections of dextrose (a 20 per cent solution) or of neoarsphenamine. Camphor, metrazol and epinephrine hydrochloride with solution of pituitary or ephedrine should be given as indicated. Transfusions may be helpful. Digitalis is contraindicated.

DOOLEY, Kent, Conn.

PARESIS AND POLYARTHRITIS FOLLOWING VARICELLA. E. NUCCI, Prat. pediat. **9**:93 (March) 1931.

Nucci reports the case of a 10 months old, breast-fed baby who had been well until it had a typical attack of varicella during an epidemic of that disease. Thirteen days after the onset, when the baby had apparently recovered, paresis of

the right arm and swelling of the right knee and ankle developed. The inflammation of the joints subsided quickly. Within one month the paretic arm was entirely normal. The author discusses the differential diagnosis at length, with especial reference to poliomyelitis.

DOOLEY, Kent, Conn.

THE BLOOD CALCIUM IN PERTUSSIS IN RELATION TO THE GALVANIC EXCITABILITY OF THE NERVES IN VARIOUS STAGES OF THE DISEASE. B. TRAMBUSTI and C. SERTORI, Riv. di clin. pediat. **29**:633 (Aug.) 1931.

In the active stages of pertussis, there is a diminution in the calcium of the blood; in the cases cited, there was from 6 to 8 mg. of calcium per hundred cubic centimeters of blood serum. This is accompaned by an increased response of the muscles to the application of a galvanic current to the nerve.

HIGGINS, Boston.

THREE CASES OF SMALLPOX FROM INSUFFICIENT VACCINATION. MARTÍNEZ VARGAS, Med. de los niños **32**:129 (May) 1931.

Improper vaccination may fail to produce immunity. The child with a small superficial scar may not have had sufficient vaccine to produce immunity. The old method of arm to arm vaccination produced immunity of long duration. Faulty technic in the newer methods may result in the absorption of insufficient vaccine, and likewise it may result in complications. Investigations have not demonstrated any true relationship between vaccination and encephalitis; with good vaccine and proper technic, encephalitis is never produced by vaccination. Three cases of smallpox are reported in children who had been vaccinated insufficiently, so that little or no immunity was present.

DWYER, Kansas City, Mo.

THE VALUE OF IMMUNIZATION AGAINST SCARLET FEVER. SCHOTTMÜLLER, Deutsche med. Wchnschr. **56**:1159 (July 11) 1930.

Scarlet fever streptococcus immune serum produces passive immunity at once. However the effect lasts only two weeks. On the other hand, scarlet fever streptococcus toxin gives active immunity beginning a few weeks after the administration and lasting two years or more. Schottmüller therefore suggests the use of both methods simultaneously in institutions where scarlet fever occurs endemically. He adopted this simultaneous method in an institution for children in Wyk-on-Fohr. In this asylum scarlet fever developed in one child four days after admission. In spite of all precautions during the next twenty days, 31 of the 223 children in this home also contracted scarlet fever; 175 of the children who remained well received 10 cc. of streptococcus immune serum and, at the same time, 1 cc. of scarlet fever toxin. Fourteen days later a second dose of scarlet fever toxin was administered. Eighteen days after the serum injection 3 cases of scarlet fever developed, and as the effect of immune serum was estimated to last for about two weeks only, another 10 cc. dose of serum was given to the previously immunized children. No further cases of the disease developed, and no harmful results have been observed from the immunization. Eighty-seven per cent of the children had a positive Dick test before immunization and only 37 per cent eight days after the third injection. If the tests had been made a longer period of time after immunization, the percentage of children reacting positively to the Dick test would probably have been even lower than 37.

The simultaneous use of active and passive immunization against scarlet fever opens a similar field in the fight against streptococci in general. The scarlet fever toxin that Schottmüller used produces an anaphylactic reaction in guinea-pigs similar to that observed clinically in scarlet fever in human beings. The author gives his hypothesis as to the mechanism of the immunization against scarlet fever.

KERESZTURI, New York.

THE DOSAGE OF ANTITOXIN IN THE TREATMENT FOR DIPHTHERIA. F. REICKE and E. REYE, Deutsche med. Wchnschr. **56**:1162 (July 11) 1930.

In the Hamburg Barmbeck Hospital much higher antitoxin doses were used in diphtheria than in the Hamburg Eppendorfer Hospital, in which combined diphtheria and streptococcus serum was given in smaller quantities. However, the therapeutic results in the two hospitals did not differ essentially from each other. Therefore the authors stress the significance of the early administration of diphtheria antitoxin rather than the amount given. The antitoxin doses in the Eppendorfer Hospital ranged from 4,200 to 7,200 units, and in the Barmbeck Hospital from 8,900 to 27,000 units. The authors quote Langer, who claimed that 200 units per kilogram of body weight is sufficient in mild cases and from 500 to 1,000 units per kilogram in severe cases. In the Eppendorfer Hospital good results were evidently obtained with far smaller doses.

KERESZTURI, New York.

INVOLVEMENT OF THE JOINTS LATE IN THE COURSE OF SCARLET FEVER. HERMANN ZISCHINSKY, Jahrb. f. Kinderh. **132**:303 (Aug.) 1931.

Among 20,000 cases of scarlet fever observed from 1902 to 1930 at the Wilhelminenspital in Vienna, there occurred 509 cases of "rheumatoid" involvement and 102 cases of the late atypical joint involvement here considered. The number of such cases was roughly proportional to the number of the rheumatoid type; there was no special age incidence. Whereas all the cases of the rheumatoid type occurred within twelve days of the onset of scarlet fever, the atypical cases occurred from the thirteenth to the forty-fourth day. The large joints, especially those of the hand and the knee, were most frequently involved; multiple involvement was observed in sixty-one cases. Pain was nearly always present; in twenty-seven cases, only pain. In twelve cases, only swelling was observed. In sixty-three cases, pain and swelling were present, with fixation of the joint in partial flexion. Effusion may occur. Mild cases last from one to two days. Severe cases may last eight days. Occasionally, recurrences are observed up to forty-one days. The process is entirely benign; endocarditis and pericarditis do not occur. (It is not clear from the text whether the author excludes from this series any case of carditis; it seems likely that he was not able to reexamine the patients after their discharge from the hospital.) Acetylsalicylic acid often caused prompt relief from pain and swelling.

CLAUSEN, Rochester, N. Y.

DIPHTHERIA: III. EXPERIENCES WITH THE SCHICK REACTION AND WITH ACTIVE IMMUNIZATION. FRIEDRICH SZIRMAL, Jahrb. f. Kinderh. **132**:323 (Aug.) 1931.

Observations on the Schick test in 1,152 children at the Stefanie Kinderspital in Budapest were:

Age	Boys		Girls	
	Number Cases	Positive Results, Per Cent	Number Cases	Positive Results, Per Cent
0– 6 months	44	4.5	26	7.7
7–12 months	22	63.6	20	60.0
1– 3 years	162	81.5	96	70.8
4– 6 years	158	68.4	128	59.4
7–10 years	134	50.7	128	43.7
11–14 years	86	32.5	114	33.3
15–20 years	10	20.0	24	41.7

The author has had a limited experience with active immunization. A critical analysis of the literature follows.

CLAUSEN, Rochester, N. Y.

DURATION OF IMMUNITY IN INTRACUTANEOUS VACCINATION. O. KIRSCH, Med. Klin. **27**:313 (Feb. *27*) 1931.

Immunity following intracutaneous vaccination is considerably less permanent than that following the usual cutaneous vaccination. The reason for this seems to be in the fact that the epidermis has less natural resistance against the virus than the intracutaneous tissues, and therefore the general and local immune reactions are stronger. The present unduly high virulence of vaccines should be decreased in the future so that unreliable methods are not resorted to.

ZENTAY, St. Louis.

EXPERIMENTAL INVESTIGATIONS ON THE SO-CALLED NEGATIVE PHASE OF DIPHTHERIA IMMUNITY. R. PRIGGE, Med. Klin. **27**:419 (March 20) 1931.

Guinea-pigs were used to decide the question that has been much discussed in recent years: whether there is any negative phase of immunity against diphtheria. The animals were immunized through the use of a commercial preparation, prepared with the addition of formaldehyde. In no animal was an increased sensitivity to diphtheria toxin or any predisposition to diphtheria infection noted. The only exception is when very high doses of the preparation are used for immunization. Even then it is not clear whether there is a true sensitivity or an injury of the animal through overdosage of the toxin. In human beings the amount injected is from 100 to 200 times smaller than that in animal experimentation. Therefore an increase of sensitivity can definitely be excluded in connection with the usual procedures.

ZENTAY, St. Louis.

RECENT EPIDEMICS OF DIPHTHERIA AND DIPHTHERIA IMMUNIZATION. E. FRIEDBERGER, Med. Klin. **27**:645 (May 1) 1931.

The author studied statistically the tendency of epidemics of diphtheria during the last decade. He uses statistics from practically all the European countries and also from the United States. The analysis of morbidity and mortality in his tables definitely shows that diphtheria has been on a decline during this time. The details of a statistical study cannot be condensed in an abstract, but the data are interesting if not entirely convincing. Friedberger also studied the effect of diphtheria immunization in American cities on the morbidity of diphtheria. He comes to the conclusion that the whole procedure has not affected the course of these epidemics to any great extent. He feels that in the whole procedure of diphtheria immunization an entirely wrong course is followed. He warns against theoretical generalizations, and feels that results obtained in animals in the laboratory cannot be applied to human beings, at least not in diphtheria. He hopes that the propaganda spreading the false notion of diphtheria immunity will subside, and also that new and better methods for treatment and prophylaxis will soon be discovered.

ZENTAY, St. Louis.

TRANSITION FORMS OF PNEUMONIA IN CHILDHOOD. EUGEN KRAMAR, Monatschr. f. Kinderh. **50**:414, 1931.

The author calls attention to the atypical pneumonias developing in children between the ages of 1 and 3 years. Both in physical signs and in symptomatology, these pneumonias have points in common with typical lobar pneumonia as well as with diffuse bronchopneumonia. Kramar offers as an explanation that at this particular age the child is undergoing a transition in the development of his immunity. Earlier his immunity is at its lowest, and diffuse pneumonia is more common. Later immunity is more permanently established and the infection is limited to pneumonia of the lobar type. The atypical pneumonias occurring between 1 and 3 years indicate a transition stage in the development of immunity.

GERSTLEY, Chicago.

VACCINE IN THE PROPHYLAXIS AND TREATMENT OF PERTUSSIS. F. GIERTHMÜHLEN, München. med. Wchnschr. **78**:271 (Feb. 13) 1931.

The diagnosis of whooping cough was made by cough culture plates and blood counts. The author found a high white cell count in the incubation period and during the active stage of the disease. Vaccine in repeated large doses (from 2 to 8 million Bordet-Gengou bacilli) in the incubation period either prevented the attack or resulted in a mild form. Local and general reactions occurred, but were mild. In the early active stage repeated doses of vaccine (from 2 to 12 million bacilli) shortened the duration of the disease and lessened the severity of the paroxysms.

BRAHDY, Mount Vernon, N. Y.

NONPROTEIN BLOOD NITROGEN IN DIPHTHERIA AND ITS PROGNOSTIC SIGNIFICANCE. JAROSLAV PROCHAZKA, Časop. lék. česk. **68**:1269 (Sept. 13) 1929.

The nonprotein blood nitrogen was found to be markedly increased in practically all cases of malignant diphtheria from the onset of the disease. Only one patient with a nitrogen content of less than 40 mg. died, while only one with a nitrogen content of more than 50 mg. recovered in a series of fifty-nine severe and fifty mild diphtheria cases. Only two cases showing a nitrogen content of 60 and 90 mg. respectively, with ultimate recovery, have been reported. The increased nitrogen is not the cause of the uremia, convulsions, unconsciousness, toxic breathing and hypertension brought on by a deviation of kidney function. In the so-called diphtheritic uremia the sensorium remains clear (in one case reported, even in the presence of 230 mg. of nitrogen), and convulsions when present are only fragmentary. Decreased diuresis in diphtheria is more likely to be due to a decreased fluid intake than to edema of the kidney. Hypertension was not present in any of the cases. Because of these observations the author feels that the designation of the complex should be azotemia and not uremia of malignant diphtheria. The early rise in blood nitrogen in the severe cases is a valuable prognostic sign.

STULIK, Chicago.

A LABORATORY INFECTION WITH SCARLET FEVER. F. VON BORMANN, Zentralbl. f. Bakt. (Abt. 1) **117**:460, 1930.

A 20 year old girl, while washing filters used in filtering cultures of streptococci from the throat washings of patients with scarlet fever, acquired an infection of the left hand. From twelve to fourteen days later typical scarlet fever developed, although the patient had not been in contact with any cases. Hemolytic streptococci, culturally identical, were obtained from the wound and from the nasopharynx. The erythema produced by the filtrate from these organisms was neutralized by scarlet fever antiserum.

CANNON, Chicago.

FURTHER EXPERIENCES WITH ACTIVE IMMUNIZATION AGAINST SCARLET FEVER. G. HERHOLZ, Ztschr. f. Kinderh. **50**:680 (March) 1931.

After trial for three years, active and passive immunization against scarlet fever is not looked on with enthusiasm by Herholz, of the Kinderheilstätle Lochstädt. He admits that the trouble may have been with the toxin used, or with the dosage. The last word, nevertheless, has not been spoken, and success is not to be attained by clinical and statistical work done in contagious hospitals, but by workers in bacteriology and immunology.

EMERSON, Boston.

IMMUNIZATION AGAINST DIPHTHERIA WITH THE PROTECTIVE SALVE OF LÖWENSTEIN. G. BLUMENTHAL and E. NASSAU, Ztschr. f. Kinderh. **50**:742 (March) 1931.

Repeated animal experiments with the antidiphtheritic salve of Löwenstein, as in the earlier studies of Otto and Blumenthal in guinea-pigs, in spite of three inunctions, gave in no case a demonstrable formation of antitoxin. Among 157 children, from 1 to 9 years old, treated twice, one became sick during the treatment and none afterward, but 35 per cent, nevertheless, still showed a positive Schick reaction. There was no increase of antitoxin demonstrated in 29 children (with one exception, which can be traced to other causes), not even in children who, before the treatment, possessed a certain antitoxin titer. With insufficient epidemiologic observation, the simultaneous consideration of the outcome of the biologic reactions (the Schick test and the determination of the content of antitoxin in the blood) makes possible a correct judgment of the result of this form of immunization.

EMERSON, Boston.

IMMUNOBIOLOGY OF MEASLES. ALOIS GUTWIRTH, Časop. lék. česk. **68**:1402 (Oct. 11); 1433 (Oct. 18) 1929.

The four fundamental reactions to infectious virus are: (1) a subthreshold infection without a biologic reaction, (2) a subthreshold infection with a latent biologic reaction, (3) a typical manifest reaction and (4) an atypical manifest reaction. The index of contagion is given as: measles, 0.95; scarlet fever, 0.4, and diphtheria, 0.1. The 3 to 14 per cent of persons considered refractory to measles in different reports may be regarded as immune after either a prenatal or subthreshold infection without manifestations. Permanent immunity may be acquired by the offspring if the mother has active measles during pregnancy, but the immunity acquired from a mother who had measles in childhood protects the infant for only four or five months after birth. The prophylactic and therapeutic measures cited in the literature are reviewed. Berkefeld filtrate from the nasopharynx of patients with prodromal symptoms of measles was incubated for ten days after treatment with 0.3 per cent formaldehyde. Then 0.1, 0.2 and 0.4 cc. were injected into the arms of twenty-one children at three day intervals. Sixteen of these have remained under observation and have not contracted measles in spite of the fact that seven of them have been definitely exposed to the disease. The small number of cases does not warrant a statement as to the definite value of this procedure.

STULIK, Chicago.

RAT-BITE FEVER. VILEM VEZER, Časop. lék. česk. **68**:1529 (Nov. 8) 1929.

Two children, aged 4 and 6 years respectively, were bitten by rats. An undulating type of fever developed in spite of Pasteur antirabies treatment. In one case spirochetes were found in the blood smears. Both children had massive engorgement of axillary and inguinal glands, though the primary lesion was on the hand. Both recovered after injections of neoarsphenamine. The incubation period of rat-bite fever is twenty-one days. Osler described a blotchy measles-like rash as one of the findings in this condition. Forty-nine definite cases have been reported, especially in China where it has been known for several hundred years. In both of the cases described, the spleen was enlarged.

STULIK, Chicago.

EXPERIMENTAL IMMUNITY WITH DIPHTHERIA ANATOXIN. B. FEIERABEND, Časop. lék. česk. **68**:1537 (Nov. 8) 1929.

In the horse a higher and more rapid development of antitoxin titer occurs with anatoxin than with toxin antigen. The author attempted to test the immunity production of various anatoxins in the guinea-pig. One injection was insufficient

to produce immunity in all guinea-pigs, though immunity developed in some after from two to six weeks. Two injections at both one and three week intervals, were sufficient to produce immunity in all animals from three to six weeks after the last injection. The antitoxic immunity derived from anatoxin in animals is sufficient to protect them against toxemia. The degree of immunity is somewhat dependent on the amount of anatoxin used. In the routine injections 0.5, 1 and 2 cc. were used, while in checking for quantity 5 cc. was used. The quantitative Schick test was used for a check-up. Anatoxins have various immunity production abilities, which may be determined by titration but not by flocculation tests. Actual antigenic ability can be determined only by experiments on the immunity of animals, such as the guinea-pig.

STULIK, Chicago.

Chronic Infections

VITAMINE D IN BONE TUBERCULOSIS IN CHILDREN. H. G. GRAYZEL, M. J. SHEAR and BENJAMIN KRAMER, Am. Rev. Tuberc. **24**:106 (Aug.) 1931.

This investigation was made on a group of eighteen tuberculous children. Seventeen had active bone tuberculosis and one tuberculosis of the skin. All were fed a diet well balanced and rich in vitamins, and were also given two tablespoonfuls of a malt and cod liver oil preparation daily. Two equal groups were formed, to one of which was given daily 4 mg. of viosterol containing 2,000 rat units per milligram during the first four months, and 7 mg. daily for the succeeding eight months. At the end of the experiment, no noticeable acceleration of the healing process was observed in the group receiving the viosterol. In spite of the relatively large doses of viosterol, no toxic symptoms or pathologic calcification developed, and there was no increase above normal in the concentration of serum calcium or of serum phosphorus.

SMITH, Ogden, Utah.

EPITUBERCULOSIS: REPORT OF AN UNUSUAL CASE WITH AUTOPSY FINDINGS. B. GOLDBERG and B. M. GASUL, Am. Rev. Tuberc. **24**:285 (Sept.) 1931.

The case reported, that of a Negro child, 6 years old, could be regarded clinically and roentgenologically as typical of the original description of Eliasberg and Neuland. The onset of the disease was subacute. There was a subfebrile temperature until the child was admitted to the hospital after a lapse of fifteen months. The cough at first was not prominent. The general condition was good in spite of the extensive consolidation of the right upper lobe. The x-ray pictures showed a dense homogeneous shadow over the involved area, pursuing the gradual, slow absorption characteristic of an epituberculous lesion. About one year after the first observation, when the patient was in good condition and there was almost complete absorption of the infiltrate, he was given a tuberculin test which was followed by a severe focal reaction. As a part of this reaction bronchial breathing occurred over the entire right lung. As focal reactions following the use of tuberculin are said to occur only in specifically affected tissue, the recrudescence of the lesion and the involvement of the lung tissue beyond the original area should definitely point out the tuberculous nature of this condition called epituberculosis. In the case reported, this conclusion was borne out by autopsy beyond any possibility of doubt. Autopsy showed caseation of the right hilar lymph nodes, with erosions of the main branches of the bronchial tree, in the lower portion of the upper lobe. This caseation and spread gave rise to the occurrence of a generalized tuberculosis.

SMITH, Ogden, Utah.

SYPHILIS: SOME PSYCHOLOGIC ASPECTS OF TREATMENT. GERALD H. J. PEARSON, Arch. Dermat. & Syph. **23**:1021 (June) 1931.

The management of a syphilitic patient presents greater problems than are encountered in the treatment of patients with other infectious diseases. 1. The

patients seem prone to refuse to accept the diagnosis and will not cooperate, and many stop treatment as soon as primary or secondary symptoms disappear. 2. The public regards the syphilitic patient as an outcast of society and so fosters fear of exposure of the nonsyphilitic person and an inferior personality in the syphilitic. 3. The married syphilitic patient fears that the marital partner will learn of the disease, and so the treatment is hindered and the relationship strained. 4. The author presents three cases in which marked behavior problems developed in children due to the strained relationship between the parents and fear of the disease on the part of the child. The child also suffers from lack of treatment, so the family life is ruined, the child is inferior, and the disease progresses. The syphilologist must treat the patient as well as the disease properly.

HENNING, Iowa City.

SYPHILITIC PAROTITIS. LOUIS CHARGIN and THEODORE ROSENTHAL, Arch. Dermat. & Syph. **24**:236 (Aug.) 1931.

Parotitis as a symptom of syphilis is a rarity, but when it does occur, proper treatment is most essential. The author reports one case and cites thirty-one cases from the literature. Parotitis may occur in early syphilis, most often up to the end of the first year of infection, as a gummatous lesion in late syphilis and as a late symptom in congenital syphilis. The enlargement may come on acutely in early stages or insidiously; it is usually bilateral. The differential diagnosis from tumors, etc., must be made by syphilitic stigmas, by the Wassermann reaction and at times only by the disappearance of the tumor, after arsenic and iodine therapy. Arsphenamine, bismuth, potassium iodide and mercury were all used with good results.

HENNING, Iowa City.

PROGNOSTIC IMPORT OF A NEGATIVE SPINAL FLUID IN EARLY AND IN LATENT SYPHILIS. H. HANFORD HOPKINS, Arch. Dermat. & Syph. **24**:404 (Sept.) 1931.

The author reports observations on 405 patients with early and latent syphilis whose spinal fluids were normal at first examination. Definite neurosyphilis developed in 2.4 per cent and questionable neurosyphilis in 1.2 per cent. He contrasted this with 15 per cent of definite and 30 per cent of questionable cases of clinical neurosyphilis that developed in a series of patients with early or late asymptomatic neurosyphilis. An originally normal spinal fluid gives an excellent prognosis except when the examination was made so early that the infection of the nervous system was not yet demonstrable.

HENNING, Iowa City.

CERTAIN PHASES OF NEPHROSCLEROSIS IN CHILDHOOD. A. GRAEME MITCHELL and GEORGE M. GUEST, J. A. M. A. **97**:1045 (Oct. 10) 1931.

There is little justification at present for the use of a complicated terminology in nephritis. In chronic nephritis the tissue of the kidney is generally involved; a pure glomerular, a pure tubular or a pure interstitial nephritis does not occur, although any one of several parts of the kidney structure may be mostly involved. Etiologic studies show: that there is a familial and hereditary predisposition; that intra-uterine nephritis may occur; that syphilis plays little part in the nephritis of early life; that acute bacterial infections may cause kidney damage, resulting in chronic nephritis; that exogenous and endogenous toxins are rare factors; that focal infections seem to have little to do with chronic kidney disease of children, and that high protein diets are not operative agents. There is no need for great protein restriction, and the better treatment consists in planning diets to meet normal requirements. Undernutrition and dwarfism commonly accompany chronic kidney disease of childhood. Peculiar bone changes resembling infantile rickets, the so-called renal rickets, occur in some cases. Further metabolic strides are needed to gain a better understanding of the marked disturbances of growth and skeletal development found in chronic nephritis in childhood.

BONAR, Salt Lake City.

THE VERNES RESORCINE TEST IN THE DIAGNOSIS AND PROGNOSIS OF TUBERCULOSIS. J. W. LOBAN and J. SMITH, Brit. J. Tuberc. **25**:11 (Jan.) 1931.

This test is made by combining resorcin with the blood serum in suspected cases and measuring the amount of precipitate or degree of turbidity by means of a photometer. Higher readings are obtained on the serums of tuberculous persons. In the authors' series of sixty-four pulmonary and extrapulmonary cases, the serial tests corresponded with the clinical course of the disease in fifty-nine, and a progressive decline in the figures obtained was found to be of prognostic value. The serums from patients with healed tuberculosis, whether pulmonary or nonpulmonary, showed low readings. Nonpulmonary cases of tuberculosis generally show Vernes readings below those obtained in pulmonary cases. In cases of bone disease in which there was extensive destruction of tissues, the readings were fairly high.

SMITH, Ogden, Utah.

INTRATHORACIC TUBERCULOSIS OF CHILDHOOD. GEORGE S. BANKS, Edinburgh M. J. **38**:145 (March) 1931.

The author is chief tuberculosis officer for Aberdeen. In the March number of this journal, which is devoted to tuberculosis, he states that difficulties of diagnosis are greatest in intrathoracic tuberculosis during school age, because of the remarkable resistance to the disease which is developing at that age. The anatomic or immunologic resistance comes on following the primary infection because of retention of bacilli in the regional lymph glands. The author believes in Parrot's law of similar adenopathies applied to tuberculosis in childhood, namely, that the infection in the lungs and a corresponding lesion in the gland adjoining will be found. He quotes Stoloff's roentgen observations verifying the association of a calcium density in the lung field, a positive tuberculin reaction and a pathologic appearance of the hilar lymph nodes, from which a diagnosis of tuberculosis within the chest might be made.

The family history is one of the most important of the diagnostic criteria, especially facts such as exposure to an infected mother. A child of such as family is not robust, showing easy fatigue, a fickle temperament, irritability and stationary weight as symptoms which are more important than cough, sputum, fever and sweats. Stigmas, such as blepharitis, phlyctenular conjunctivitis, nail biting and clubbing of fingers, when found in such children suggest tuberculosis. The results of physical examination must be interpreted by physicians who are constantly in the habit of examining children. Much doubt arises about the standards for percussion and ausculation. The normal higher pitch from both percussion and breath sounds, in the right interscapular region, makes it difficult to discover enlarged tracheobronchial glands, which are more numerous in that area. The Eustace Smith bruit might be an important sign if its normal presence could be ruled out. The spinal sign of sinking of the mid-dorsal spines (usually the fifth to the seventh) and changes of percussion and auscultation sounds over these may be helpful. D'Espine's sign, however, is rarely possible of demonstration. Roentgen examination he thinks helpful, but it is often misleading and the same film may find a wide variety of interpretation by different observers.

When signs are vague and latent, the diagnosis in children rests chiefly on roentgenography. Preventorium treatment, Banks thinks, is indicated more because of prolonged contact with an open case and also because of a positive skin test. Although enlarged glands in the chest may be demonstrated by roentgenograms, one should determine whether they are actively tuberculous. The author feels that only a small percentage of children with such enlarged glands have progressive pulmonary disease in later life. The lesions typical of childhood may persist in adult life, and death at that time may reveal tuberculosis of childhood, the "primary complex." Therefore, it is a picture different from the apical tuberculosis of adults. It shows the toxic features of tuberculosis and the resulting stigmas, without the clearcut manifestations found in adult pulmonary tuberculosis with tubercle-laden sputum.

NEFF, Kansas City, Mo.

LUPOID SYPHILIS. J. GATÉ, P.-J. MICHEL and C. E. BOYER, Bull. Soc. franç. de dermat. et syph. (Réunion dermat. de Lyon) **38**:1203 (July) 1931.

A girl, aged 9 years, had a lesion on the right thigh of several years' duration. It consisted of a violaceous plaque, ulcerating at two points and showing nodules under the diascope. Inguinal adenopathy was present. A clinical diagnosis of lupus seemed plausible. However, the child had certain stigmas of congenital syphilis and a slightly positive Wassermann reaction of the blood, and the lesion melted away under antisyphilic treatment. Thus one was justified in changing the diagnosis in this case to lupoid syphilis.

GANDY, Houston, Texas [ARCH. DERMAT. & SYPH.].

RECURRING HERPES AND CONGENITAL SYPHILIS. J. WATRIN, Bull. Soc. franç. de dermat. et syph. (Réunion dermat. de Nancy) **38**:1075 (July) 1931.

Two children with congenital syphilis also had recurring herpes simplex of the face, the latter disease being cured by antisyphilitic treatment. Watrin believes that this was due to the "shock" of the arsenical injections, after the manner of nonspecific protein therapy.

GANDY, Houston, Texas [ARCH. DERMAT. & SYPH.].

THE SIGNIFICANCE OF VARIATIONS IN THE SPINAL FLUID IN TUBERCULOUS MENINGITIS. A. LEONE, Riv. di clin. pediat. **29**:655 (Aug.) 1931.

A report is given of a patient with generalized miliary tuberculosis, characterized by meningeal symptoms and anuria. Lumbar puncture showed a xanthochromic fluid, which coagulated in a few minutes; not only was the fibrin content high (1.2 per cent) but also the total albumin (15 per cent). A necropsy was obtained. The anuria was apparently due to a spasm of the sphincter caused by the presence of a tubercle in the trigone. The spinal fluid changes, indicating the Froin type of meningitis, are found in cases of miliary tuberculosis, in which there is interference with the flow of the spinal fluid by occlusion with bacillary emboli.

HIGGINS, Boston.

GIARDIASIS IN INFANCY. ENRIQUE J. SAUBIDET, Rev. méd. latino-am. **16**:993 (April) 1931.

Intestinal parasitic infections are prevalent in Argentina. Seventy-six per cent of 135 children examined were affected. The most common parasites are Giardia intestinalis and Blastocystis hominis. The frequency of amebiasis and the relative infrequency of round worm, whip worm and tapeworm infections is noteworthy. Giardiasis is more frequent in children than in adults. Symptoms commonly found are referable to the digestive tract and associated glands: diffuse abdominal pain, a protuberant abdomen, frequently pain in the right upper quadrant and constipation. Diarrhea is uncommon, but a painful enlarged liver with slight icterus is sometimes observed. In severe cases nervous symptoms, such as irritability and headache, occur.

DWYER, Kansas City, Mo.

TREATMENT FOR CONGENITAL SYPHILIS IN INFANCY WITH ACETARSONE BY MOUTH. H. VON METTENHEIM, Med. Klin. **27**:422 (March 20) 1931.

Internal treatment for congenital syphilis, if it is in any way reliable, has certain advantages over the treatment by injections. Von Mettenheim tried acetarsone, the preparation recommended by Levaditi. In this paper he reports only a small series of eighteen cases in which this method was used. The influence on the general condition of the children and also the effect on the central nervous system seem to be encouraging. The dosage varied from 0.01 to 0.25 Gm., depending on the size and age of the child. It is best to begin with

small dosage and increase it gradually. One course of treatment lasted from sixty-three to one hundred and seventy-five days, followed by an intermission. Serologic control of the blood and cerebrospinal fluid is advised as in other forms of treatment. Seven of eighteen cases gave a negative Wassermann reaction after the use of acetarsone in a total amount ranging from 1.5 to 33 Gm. The average total dosage in these cases was 13.3 Gm. For the best results, early treatment is suggested. Early preventive treatment is suggested for all children whose mothers show syphilis in the absence of clinical signs. The length of treatment needed for a complete cure cannot be definitely decided at this phase of the investigation.

ZENTAY, St. Louis.

EXPERIMENTAL INVESTIGATION ON THE EFFECT OF ACETARSONE IN SYPHILITIC INFECTION OF THE CENTRAL NERVOUS SYSTEM. H. HORSTER, Med. Klin. **27**:511 (April 2) 1931.

White mice were used in the experiments. They were infected in the usual way by the implantation of chancre tissues. Early treatment was started the next day after infection; late treatment, after fifty-six days. Acetarsone was given through a small stomach tube. The dosage was 10 mg. per twenty grams of body weight, ten times a day, every second day. The brains of the animal were tested for spirochetes by injections into other animals. The results show that early treatment, if continued for a sufficiently long time, prevents syphilitic infection of the central nervous system of white mice, and also that through this medication the infection already developed can be cured.

ZENTAY, St. Louis.

BLOOD CHANGES IN SYPHILIS. PAUL NEUDA, Wien. Arch. f. inn. Med. **21**: 455 (July) 1931.

The clinical experience of the tolerance of the syphilitic patient to iodides points to a possible qualitative change in the body fats brought about through the influence of the infection. Chemical analysis of the blood fat in both normal and syphilitic persons seems to substantiate this conception. In the syphilitic patient a relatively and absolutely increased content of phosphatides as compared with the total fat was consistently found. In some cases a marked increase of total fat was found. The determination of the iodine number gave a high increase in unsaturated fatty acids in the syphilitic patient. Both of these findings are important, since there is a definite interdependence between these factors. Any marked qualitative change in blood fat predisposes to the increased formation of unsaturated fatty acids.

SCHLUTZ, Chicago.

THE TERMINAL STAGES OF PULMONARY TUBERCULOSIS IN CHILDREN. D. SCHENKMANN and V. RUSSATJE, Ztschr. f. Kinderh. **51**:309, 1931.

The terminal forms of pulmonary tuberculosis in children, whether typical phthisis or the galloping forms, are different from those in adults. In early childhood are seen the stormy exudative processes in caseous pneumonia or acinous glandular forms and uninterrupted miliarization of the lungs and other organs. By contrast, at school age, prolonged forms with a tendency to the formation of large cavities are noted. The dynamics of the juvenile organism suffer, as is recognized by the diminished resistance and expressed by a change in the leukocyte formula and an increase in the precipitation time, in the hectic temperature and in the disturbances of the vegetative nervous system. As a rule, tubercle bacilli are found in the sputum and in the stool in cases with a fatal outcome. The tuberculin reaction, especially that of Mantoux, is usually positive; it is negative only in cachexia and in the preagonal stage. The most frequent complications are adhesive pleuritis and ulceration of the intestine, the latter being first found at autopsy.

EMERSON, Boston.

INTRALUMBAR TUBERCULIN THERAPY IN BASILAR MENINGITIS. A. HOCHWALD and O. SAXL, Ztschr. f. Kinderh. **51**:656, 1931.

A report is made of eight cases of basilar meningitis in which intralumbar tuberculin therapy was used, but could not prevent death. Two patients died within twenty-four hours following the injection; this was thought to have been due to an allergic reaction. Two cases showed a long remission, and two cases a flaring up of the Pirquet reaction, which was looked on as due to a transference of the immune bodies from the spinal fluid into the blood. It is noted that many clinical and pathologico-anatomic results of intradural tuberculin treatment, such as fever, hyperemia, edema, a cellular exudate from the meninges, acute changes in the neighborhood of the malpighian bodies of the spleen and a reaction of the reticulo-endothelial system, can be reproduced in experimental animals. There is a possibility that the processes going on in the spinal canal are nonspecific.

EMERSON, Boston.

THE CALMETTE-GUÉRIN VACCINATION METHOD. T. MADSEN, Ugesk. f. læger **93**:553 (May 21) 1931.

In his short résumé, Dr. Madsen considers it settled that the vaccine does not in any way change into a virulent state. The time is not yet ripe for the general use of this method; more careful work and further statistics are needed. Children and infants definitely exposed to open cases should be given the vaccine and kept in institutions until the vaccination has "taken" and positive tuberculin tests have been obtained.

ELGHAMMER, Chicago.

WASSERMANN REACTION IN CHILDREN TREATED FOR CONGENITAL SYPHILIS. L. B. LAURITZEN, Ugesk. f. læger **93**:665 (June 18) 1931.

Repeated series of antisyphilitic treatment produced negative Wassermann reactions in 99 per cent of 182 children treated at the Welander Home. The author thinks that it is most important to continue treatment after the disappearance of symptoms until a negative Wassermann reaction is obtained.

ELGHAMMER, Chicago.

Internal Diseases

A CASE OF CONGENITAL STENOSIS OF THE PULMONARY VALVE, WITH LATE ONSET OF CYANOSIS: DEATH FROM CARCINOMA OF THE PANCREAS. JOHN H. ARNET and CHARLES FRANCIS LONG, Am. J. M. Sc. **182**:212 (Aug.) 1931.

A man, aged 33, died of carcinoma of the pancreas, complicating a simple congenital pulmonary stenosis. He had not been a blue baby, nor did his early life indicate anything abnormal. He was athletic, saw service in the World War and worked hard as a truck driver. He gradually developed localized areas of cyanosis within the skin, due to vascular stenosis, a not uncommon finding in congenital heart disease. Significant autopsy findings are reported, along with the patient's history and progress.

HENSKE, Omaha.

FURTHER STUDIES IN A CASE OF CALCIFICATION OF SUBCUTANEOUS TISSUE ("CALCINOSIS UNIVERSALIS") IN A CHILD. WALTER BAUER, ALEXANDER MARBLE and GRANVILLE A. BENNETT, Am. J. M. Sc. **182**:237 (Aug.) 1931.

A follow-up report of a case of "calcinosis universalis" is given. Calcium and phosphorus balance studies are presented showing a tendency to retain absorbed calcium and phosphorus, especially the former, even though blood calcium and phosphorus values were normal. Interesting pictures of the child, roentgenograms and photomicrographs are included. Biopsy revealed calcium and phosphorus in

the amount and ratio commonly found in adult bone and in pathologic human calcification. Ammonium chloride acidosis produced an increase in the urinary output of both calcium and phosphorus.

HENSKE, Omaha.

PHYSIOLOGIC RESPONSES AND IMMUNE REACTIONS TO EXTRACTS OF CERTAIN INTESTINAL PARASITES. HIRAM E. ESSEX, J. MARKOWITZ and FRANK C. MANN, Am. J. Physiol. **97**:18 (Aug. 1) 1931.

A study was made of extracts of various parasitic worms with regard to their effect on blood pressure. Dogs were used in this experiment. The vasomotor action (depressant) of the extracts was comparable to that of bee venom or rattlesnake venom, but differed in that they did not produce hemolysis or diffuse hemorrhage. Taenia pisiformis extracts, which were markedly depressant in dogs not previously infested, had no effect on the blood pressure of dogs that were heavily infested. Thus, it appears that the parasites harbored by dogs elaborate substances against which the host develops immunity, and that when immunity has developed, the dog remains infested, but subsequently is not greatly injured by the parasites.

NOURSE, Cleveland.

THE ENDOCARDITIC PROCESS IN CHILDHOOD. BINDO DE VECCHI, Arch. Path. **12**:49 (July) 1931.

The author believes that the endocarditic process in children is much more frequent than it has hitherto been considered. The reason for its apparent infrequency is that attention has been paid to gross changes only and that significant histologic changes have been overlooked. The author has made a study of these in forty-two cases. He concludes "that inflammatory processes of marked intensity often take place in young children affected by various toxic infective diseases, but that the subsequent process of thrombosis often fails to appear; thus microscopic diagnosis of such lesions at autopsy is almost impossible. These are lesions of particular importance both for the inferences that can be drawn from them about the pathogenesis of the endocarditic process in general, and on account of the sequelae to which their further development gives rise in establishment of valvular defects, the mode of origin of which has been obscure."

LESLIE, Evanston, Ill.

THE TREATMENT OF THE NEPHROTIC SYNDROME. JOSEPH K. CALVIN and A. H. GOLDBERG, Arch. Pediat. **48**:485 (Aug.) 1931.

The authors give their results in the treatment for the nephrotic syndrome. Twelve cases are presented. Ten of these cases presented the following findings: (1) cyclic pitting edema of the shifting type (the edema fluid was very low in protein content and easily obtained by puncture of the skin), (2) proteinuria (usually marked and consisting largely of albumin), (3) lowered plasma proteins with a reversal of the albumin-globulin ratio, (4) lipemia and lipoidemia, (5) doubly refractive lipoids in the urine and (6) an absence of hematuria, hypertension and impaired renal function. Two cases had the features mentioned, and in addition showed hematuria, hypertension, impaired renal function or a combination of these. The authors review and summarize what is known and surmised concerning the pathogenesis of edema.

In the treatment for the edema occurring in these twelve cases, an attempt was made to raise the plasma proteins by the feeding of high caloric diets and the administration of blood transfusions. Foci of infection were eliminated when present. Salt was restricted to 2 Gm. or less daily, and fluids were restricted. Various diuretics were used. It was felt that the most satisfactory procedure, at least during the stage of marked edema, was the combined use of a high protein diet, low salt diet and low fluid diet, with one or more of the diuretics. Evaluation of the various therapeutic procedures proved difficult because of the cyclic nature of edema.

WADDELL, University, Va.

SPONTANEOUS PNEUMOTHORAX IN INFANCY: REPORT OF CASE. S. J. McCLENDON, Arch. Pediat. **48**:511 (Aug.) 1931.

A case of spontaneous pneumothorax following bronchopneumonia is reported.

WADDELL, University, Va.

NEPHROSIS (EPSTEIN): REPORT OF CASE WITH RECOVERY IN BOY TWO AND ONE-HALF YEARS OF AGE. WALTER F. BOPP, Arch. Pediat. **48**:516 (Aug.) 1931.

A case of nephrosis is reported in which the patient was successfully treated with a diet high in protein, thyroid extract and thyroxine. The author believes the condition to be extrarenal and probably metabolic in origin. A survey of the literature concerning nephrosis accompanies the report.

WADDELL, University, Va.

LEUKEMIC BLOOD PICTURE WITH ROENTGEN CHANGES IN THE BONES. ROLLA G. KARSHNER, California & West. Med. **35**:125 (Aug.) 1931.

Six cases are reported, one in detail, of children with leukemic blood pictures, showing in all instances similar changes in the bones in roentgenograms: a finely porous destruction, gross destructive lesions and periosteal proliferation. Autopsy, performed in four of the cases, showed lymphatic infiltration within the internal organs and bones.

DICKEY, San Francisco.

NOTES ON THE RELATION OF IODINE TO GOITRE. J. F. McCLENDON, Endocrinology **15**:281 (July-Aug.) 1931.

The work of Marine showing that iodide is a prophylactic against goiter in children has been continued in Switzerland with similar results. An interesting comparison is made of two neighboring cantons, each of which has a government salt monopoly. The salt used in the canton of Freiburg has a much lower iodine content than that used in Vand, and the incidence of goiter is considerably higher in Freiburg. In Minnesota, which is a highly goitrous state, the iodine in local foods was found to be very low, whereas the New England coast produces foods high in iodine. The state of South Carolina, where goiter incidence is low, produces vegetables with a high iodine content. Remington's figures show that Minnesota potatoes contain 86 parts, and Carolina potatoes 211 parts of iodine per billion. The reason for this appears to be the fact that Minnesota was glaciated and the glaciers removed the soil, which probably was high in iodine, and dumped sand and gravel over the state. Sandy soils are lower in iodine than clay soils of the same region. It has been shown that in Switzerland the incidence of goiter is higher in German than in French families; this is attributed to the fact that the German cook boils the vegetables in several changes of water, throwing out the iodine with the water. Hence, proper cooking is as important as the high original iodine content of foods. The author concludes that no quantitative relationship of iodine to goiter has been worked out, and he suggests that different forms of iodine may have different effects. To eliminate goiter, a change in food habits must be adopted by the general population.

JACOBSEN, Buffalo.

FAMILIAL HYPOTHYROIDISM. E. KOST SHELTON, Endocrinology **15**:297 (July-Aug.) 1931.

A family of four children is described all of whom suffered from hypothyroidism of the type that frequently remains undiagnosed. None had visible goiter, myxedema or obvious cretinous degeneration. All were undersized and had exaggerated lordosis, retroussé noses, prominent abdomens and malocclusion. The basal metabolic rates of the two older children averaged minus 25. All showed

definite retardation in development of carpal ossification centers. On thyroid medication all grew rapidly in height, and the carpal centers appeared at an accelerated rate. The father of the children was normal from the endocrine standpoint. The mother had a basal metabolic rate of minus 40 and had suffered for many years from asthma, hay fever and hypersensitiveness of the rhinal mucous membrane. The taking of thyroid extract was found to relieve these symptoms effectively; they recurred when the thyroid extract was omitted.

JACOBSEN, Buffalo.

IDIOPATHIC APLASTIC ANEMIA. J. HAROLD ROOT, New England J. Med. **203**:1225 (Dec. 18) 1930.

A case of idiopathic aplastic anemia in a boy of 9 years is described; a full pathologic report is included. The course, clinical features and postmortem findings made the diagnosis quite reliable. Idiopathic aplastic anemia is less common than other forms, and there is no destruction of blood. The color index is usually less than 1; however, this is not always true. White cells are reduced, and there is a relative increase in the small lymphocytes. Coagulation time is lengthened. There is a gradual onset with malaise, anorexia and progressive pallor. The prognosis is poor. The duration is usually a few weeks. X-rays may be used.

GENGENBACH, Denver.

PROGNOSIS IN BRONCHIECTASIS. LEONARD FINDLAY, Arch. Dis. Childhood **6**:1 (Feb.) 1931.

Fourteen cases were observed over periods of three years or longer. In three cases the condition disappeared, but in these the dilatation was slight. In three cases the condition remained unchanged, and in eight cases it grew steadily worse. The author concludes: 1. The prognosis in bronchiectasis in childhood is grave, as the condition usually gets worse steadily, and leads to a fatal termination. 2. Undoubted bronchiectasis following chronic pneumonia may disappear, but only when the degree of dilatation is slight. 3. The age of onset of the bronchiectasis would seem to influence the course of events: Recovery is more probable in the cases that develop during later childhood. 4. During childhood the duration of the illness is of no prognostic help.

KELLY, Milwaukee.

THE ONSET OF ACROMEGALY BEFORE FIFTEEN YEARS OF AGE. F. R. B. ATKINSON, Brit. J. Child. Dis. **28**:121 (April-June) 1931.

The author gives very brief descriptions of thirty-two cases of alleged acromegaly collected from the literature. The ages of the patients range from 6 to 14 years of age. Seven of the cases he rejects for one reason or another. The article throws no new light on the subject.

LANGMANN, New York.

RICKETTSIA-LIKE BODIES IN RHEUMATIC CARDITIS. J. TERTIUS CLARKE and MACKENZIE DOUGLAS, Brit. M. J. **2**:247 (Aug. 8) 1931.

The authors recount the finding of Rickettsia-like bodies, usually in the Aschoff bodies at the margin of the muscle bundles, in rheumatic carditis. These are found only with the Leishman and Giemsa stains. They have been found in eight cases of rheumatic heart.

ROYSTER, University, Va.

OBSERVATIONS ON THE BLOOD CHEMISTRY IN OSTEOMALACIA. T. A. HUGHES, D. L. SHRIVASTAVA and P. M. SAHAI, Indian J. M. Research **17**:470, 1929.

In treated patients with osteomalacia a low calcium content was found when the response to treatment was poor or when treatment had been of short duration.

Improvement was usually associated with a normal or high serum calcium. The inorganic phosphorus was normally lower in untreated than in treated patients. Low values for blood cholesterol were found in most of the patients examined.

KUGELMASS, New York.

NON-SPECIFIC TREATMENT OF ASTHMA. A. GUNN AULD, Lancet **1**:804 (April 11) 1931.

Good results are reported in the treatment for asthma by the use of serum peptone. Peptone is added to the patient's own blood serum and this is incubated. Beginning with 5 minims (0.3 cc.) of the 5 per cent solution of peptone, the dosage is increased up to 2, 2.5 or 3 cc., if suitable, the injections being given intravenously twice a week. In thousands of injections the author has not found this method dangerous, even in young children. He reports that in a good many patients after treatment the asthma has been practically or entirely absent for three years.

LANGMANN, New York.

THE SPLEEN: ITS STRUCTURE, FUNCTIONS AND DISEASES. J. W. MCNEE, Lancet **1**:951 (May 2); 1009 (May 9) 1931.

The author's comparative studies of the spleen of animals proved of great help in elucidating some of the problems of the complex human spleen. Among the more important anatomic features mentioned are the splenic trabeculae which in man are the only structures of the spleen which contain muscle tissue. These are of critical importance in relation to the contractility of the organ. The lobularity of the spleen is a most important fact to take note of and one which affects many pathologic processes. Even in man a tendency to lobularity can be made out by special methods of staining. Valdoni's studies of the circulation of the spleen (1929) have proved enlightening. The comparative studies of the author and Cashin proved that the circulation was different in different animals.

"On the evidence available at present, I submit that our best working hypothesis, agreeing with many obscured facts, is to regard the circulation through the human spleen as twofold. The first, or ordinary circulation going on continually, is a direct one, the blood being pumped through the splenic artery into venous sinuses, and from thence passing directly into the veins. The second circulation is intermittent, brought about by contraction and relaxation of the whole organ, and consists of an emptying of the pulp spaces through the wide stigmata into the veins and a filling again through the lateral channels in the walls of the ellipsoids."

So far as knowledge has gone the spleen may contract both by enzyme action (epinephrine) and by the influence of central nervous control.

"On the whole it seems probable that the reticulo-endothelial system of cells is in some way connected with the processes of immunity to infection, and so the spleen, as the chief source of these cells, must be regarded as important."

The author's general classification of diseases of the spleen is as follows: (1) abnormalities: congenital and acquired; (2) infections: acute, granulomatous, parasitic; (3) diseases affecting the myeloid and lymphatic elements; (4) diseases affecting the reticulo-endothelial elements; (5) diseases affecting the vascular system; (6) tumors: simple, malignant (primary and metastatic); (7) combined diseases of the spleen, liver and hematopoietic system (Eppinger's "hepato-lienalen Erkrankungen") and splenic enlargement in hepatic cirrhosis.

LANGMANN, New York.

CHRONIC RESPIRATORY INFECTIONS IN CHILDHOOD. GUY SPRINGTHORPE, M. J. Australia **1**:649 (May 30) 1931.

A comparison is made between tuberculous and nontuberculous infections. The mode of infection and the pathology of the childhood type of tuberculosis are

reviewed. The difficulty of diagnosis in tracheobronchial tuberculosis and the need for carefully coordinating roentgen with clinical signs are emphasized. The necessity for the careful watching of school children is shown by Chadwick's studies in Massachusetts. The author feels that similar conditions prevail in Australia. In the nontuberculous infections the pathogenesis of pulmonary fibrosis is reviewed. The importance of thoroughly examining the whole respiratory tract, even though symptoms and signs are confined to the lungs, is reemphasized.

TENNEY, Madison, Wis.

GENERAL ENLARGEMENT OF LYMPH GLANDS. SPLENOMEGALY. ENLARGEMENT OF HEAD WITH OEDEMA OF FACE. GEOFFREY L. S. KONSTAM, Proc. Roy. Soc. Med. **24**:703 (April) 1931.

At 6 weeks of age, a child was noticed to have a very large head, and at 9½ months he was admitted to the hospital where a tentative diagnosis of generalized glandular tuberculosis was made, based on a biopsy report on an excised gland. The Wassermann reaction was negative. After the patient's discharge from the hospital the abdomen began to enlarge, but the swellings seemed to grow less. A year later the masses began to increase rapidly in size, and the eyelids and face became swollen. For six weeks the child was urgently dyspneic. He was admitted to the hospital again at 3½ years of age with great edema of the eyelids, face and neck; the circumference of the head was 21½ inches (54.6 cm.). There was great enlargement of the submaxillary supraclavicular and axillary glands. The glands spread in size from that of a grape to that of an almond. The pulse rate was 120 per minute and a systolic murmur was heard at the base and apex. Ascites was present. The respirations were noisy, and the spleen was enlarged. The urine showed a trace of protein as globulin and mucin. Pyrexia was present. A roentgenogram of the skull showed a woolly appearance; the calvarium was thicker than normal, and one side of the chest showed dense shadows to the right of the mediastinum, extending beyond the right border of the heart. The report is accompanied by a full blood picture.

WILLIAMSON, New Orleans.

GAUCHER'S DISEASE VERIFIED BY SPLENIC PUNCTURE. LEONARD FINDLAY, Proc. Roy. Soc. Med. **24**:848 (May) 1931.

A patient, aged 13½ months, was admitted to the hospital acutely ill, with rigidity of the neck and retraction of the head. The spleen and liver were much enlarged. Examination of the blood showed: hemoglobin, 70 per cent; red blood cells, 5,670,000; white blood cells, 10,000; polymorphonuclears, 52 per cent; lymphocytes, 48 per cent, eosinophils, 5 per cent, and myelocytes, 1 per cent. The Mantoux and Wassermann tests were negative. Small pieces of splenic tissue showed typical foamy Gaucher cells with an alveolar arrangement. A roentgenogram of the spine showed a fuzziness about the vertebrae in the mid-dorsal region.

WILLIAMSON, New Orleans.

ENLARGEMENT OF LIVER? SARCOMA. HILDA N. STOESSIGER, Proc. Roy. Soc. Med. **24**:858 (May) 1931.

A girl, aged 4 years, was well until four weeks previous to her admission to the hospital. At that time she complained of vague abdominal pains. Swelling of the abdomen was noticed by the parents about six days before admission. On examination the enlargement of the abdomen seemed generalized, but there was marked bulging to the right of the falciform ligament. The organ felt firm and the surface was smooth except posteriorly in the loin where there was a nodular mass. No ascites was found. Small shotty glands were found in the groins and the axillae and in the anterior and posterior angles of the neck. The Wassermann reaction of the blood was negative. A roentgenogram of the chest showed no metastases.

WILLIAMSON, New Orleans.

FRÖHLICH'S SYNDROME AND HEMOPHILIA. HILDRED CARLILL, Proc. Roy. Soc. Med. **24**:1050 (June) 1931.

A boy, 10 years old, had bled and bruised readily since infancy. Delivery had been difficult. He had had considerable hemorrhage when the first teeth were shed (Jan. 11, 1931). After he fell and cut his right temple he was admitted to the hospital. A large hematoma formed which took weeks to absorb. He had the typical appearance of Fröhlich's syndrome. He could not read or write. The sella turcica was small. The blood picture is given in the report. The author suggests that there may have been a hemophilic hemorrhage into the region of the pituitary gland at birth.

WILLIAMSON, New Orleans.

HEMOPHILIC JOINT WITH GLANDULAR ENLARGEMENT. C. PRICE THOMAS, Proc. Roy. Soc. Med. **24**:1052 (June) 1931.

A case was reported in a boy of 10 years. On admission to the hospital his right knee was swollen. Blood was oozing from the gums. There were palpable glands in the neck and groin which became larger during his stay in the hospital. The spleen was palpable. The boy suffered from chronic otitis media. Bleeding time was thirteen minutes, and clotting time forty-five minutes. The blood count showed a secondary anemia. There was no doubt that the boy had hemarthrosis. He had had profuse hemorrhages, and had been operated on at another hospital for a supposed osteomyelitis. At operation a blood clot was found.

WILLIAMSON, New Orleans.

TACHYCARDIA: "NERVOUS HEART." W. G. WYLLIE, Proc. Roy. Soc. Med. **24**:1053 (June) 1931.

A boy of 9 years was taken to the hospital because of fear of the dark, night terrors and lienteric diarrhea. Nothing was found on physical examination except an extremely rapid pulse rate (from 120 to 160), a widely diffuse apex beat and marked suprasternal pulsation. The blood pressure was 110 systolic and 70 diastolic. Electrographic tracings showed no abnormality. At rest in bed the pulse rate varied between 94 and 116. The tachycardia appeared to be induced entirely by fear and nervousness.

WILLIAMSON, New Orleans.

FOUR CASES OF FRAGILITAS OSSIUM AND BLUE SCLEROTICS. R. W. B. ELLIS, Proc. Roy. Soc. Med. **24**:1057 (June) 1931.

Fragilitas ossium and blue sclerotics were noted in four patients aged respectively 3½, 2, 8 and 14 years. The reports are accompanied by genealogical tables.

WILLIAMSON, New Orleans.

DIFFERENTIAL DIAGNOSIS OF PERIODIC VOMITING WITH ACETONEMIA AND RECURRENT VOMITING OF DUODENAL STENOSIS. A. B. MARFAN, Arch. de méd. d. enf. **34**:397 (July) 1931.

Cyclic vomiting, usually appearing between the first and sixth year and characterized by obscure deviations of metabolism resulting in the production of toxic substances, which in turn induce vomiting and the appearance of ketone bodies in the urine, practically always disappears spontaneously and permanently between 11 and 13 years of age.

While the pathogenesis of this disorder is still somewhat obscure, it has been a common observation that it is a manifestation of a diathesis known among French clinicians as heredo-arthritic, and the phenomena noted during an attack have been attributed, without sufficient proof, to an anaphylactic shock. Among children so disposed, various factors have been considered as exciting agents; among these may be noted overfeeding, especially of foods with a high fat content; obstinate

constipation; dentition; drastic purgation, as with calomel; the administration of certain drugs, such as those with the salicylic radical; anesthesia from ether or chloroform; a cerebral commotion of traumatic origin; lumbar puncture and the onset of certain diseases (eruptive fevers, pneumonia, meningitis and appendicitis). So far as the latter is concerned, Marfan has previously shown that the association of cyclic vomiting with acute or chronic appendicitis is not tenable for the convincing reason that many patients continue to have their vomiting attacks after ablation of the appendix, although it is admitted that the differential diagnosis between an appendiceal crisis and an attack of recurrent vomiting is sometimes difficult; the attacks may, of course, occur simultaneously and thus confuse the most sagacious clinician.

A novel explanation for these bouts of vomiting was recently advanced by Camera, of the University of Turin. He maintained that these attacks are a part of the clinical picture produced by a particular variety of duodenal stenosis following errors in development; the vomiting is due to compression of the horizontal portion of the duodenum by the pedicle of the mesenteric vessels, the result of a congenital anomaly in which there has been a general retardation in the union of the leaves of the right mesentery or mesocolon, the ascending mesocolon and the right half of the transverse mesocolon. This anatomic defect gives undue mobility to the structures involved and permits traction on the pedicle of the mesenteric vessels as it crosses the anterosuperior surface of the third portion of the duodenum, and consequent narrowing of the tube. If one accepts this view, it is clear that, according to the degree of constriction and the permanency of the pull, the clinical picture will change; if constipation exists, the increased weight of the unsupported intestine is supposed to favor an attack. This anomaly of the right mesentery is found more commonly among boys than girls, and may be complicated with megacolon.

It is extremely difficult to conduct a roentgen examination during a crisis, but observations have been made in two cases: In the one reported by Duval and Roux, there were violent peristaltic movements of the stomach and duodenum, with dilatation of the latter structure up to the middle of the horizontal portion; in the case described by Camera, the stomach was enormously dilated, depressed and nearly filled with liquid; under external pressure the barium mixture was seen to traverse the pylorus and to fill the duodenum up to the third portion where it was arrested. If dorsal decubitus was observed, the mixture returned to the stomach. Roentgenograms have also been made between attacks. In the case of Duval and Roux the structures in the upper part of the abdomen appeared entirely normal; in the case of Camera, however, and in still another instance reported by R. Miller and Courtney Gage, evidences of duodenal stenosis still persisted.

Stenoses in this portion of the intestine, with violent vomiting, may be due not only to compression by the pedicle of the mesenteric vessels but to torsion or narrowing by fibrous bands, relics of fetal peritonitis or postnatal causes, such as syphilis, duodenal ulcers and intestinal stasis. Several observers, among whom may be noted Kleinknecht, Specklin and Vonderweidt, Hayes and Shaw, Reginald Miller and Ombredanne, have reported this syndrome from the cicatrix of an old ulcer. Operation in several cases, either gastro-jejunostomy or duodeno-jejunostomy, has relieved the condition completely. In spite of this evidence, Marfan challenges the theory that all cases of periodic vomiting with acetonemia have an anatomic origin. He points out that in frank cases of duodenal stenosis, the patients usually suffer, between attacks, from dyspepsia, loss of appetite and constipation; they complain of pain, usually about the umbilicus. Among children, however, subject to attacks of what is designated as cyclic vomiting, few, if any, suffer from any of these symptoms between attacks; their appetite is good, often unusually good; many of them are regular at stool and practically none complains of abdominal pain. Acetonemia is a constant factor in the clinical picture, and may often even precede an attack, so that if one is alert, the seizure is aborted or wholly prevented. It would be difficult to explain this early appearance of ketosis, if periodic vomiting were due exclusively to stenosis of the duodenum; it is also

difficult to comprehend why these attacks cease at puberty, if anatomic anomalies are the most important etiologic factors, and, finally, it is obvious that the successful management of periodic vomiting in childhood through the use of alkalies and abstention from fats could not possibly obtain if the origin of the disease was embraced solely in duodenal stenosis.

Marfan has made fifteen roentgen studies, and in no case has he found evidences of distortion or narrowing of the upper intestine; he concludes with the assertion that these are two distinct diseases, and he outlines various methods of individual recognition.

AMESSE, Denver.

ANURIA IN A CHILD, WITH RECOVERY. MAURICE LEVY and GRAND, Gaz. d. hôp. **104**:1085 (July 15) 1931.

A boy, 10½ years old, was operated on for appendicitis during the first twenty-four hours of the attack. For five days he seemed to convalesce normally; then he suddenly complained of abdominal pain, and vomited two or three times. His urine was distinctly bloody. In the next two days complete anuria developed; catheterization gave negative results, and the bladder could not be palpated. The vomiting became worse. The blood urea amounted to 355 mg. per hundred cubic centimeters. After four days of complete anuria a transfusion (100 cc.) was given, and the next morning the patient voided 250 cc. of normal urine. In five days he recovered completely. The onset seemed to be late for reflex anuria. The negative urinary finding after transfusion and the fact that the temperature was constantly below 38 C. (100.4 F.), with no evidence of scarlet fever, made a diagnosis of nephritis questionable. The fact is interesting that the plasma chloride did not fall below 313 mg. (chlorine and not sodium chloride) in spite of frequent vomiting, although saline solution was given only on the last day of the anuria.

KAJDI, Baltimore.

BACTERIOLOGIC STUDY OF BRONCHOPNEUMONIAS AND TREATMENT BY VACCINOTHERAPY. ANDRÉ DUFOURT, Union méd. du Canada **60**:531 (Aug.) 1931.

Professor Dufourt gives an excellent résumé of the history of the study of bronchopneumonia. This paper is, in part, taken from his report to the Lausanne Congress of Pediatrics in 1927. Bacteriologic studies have shown the pneumococcus to be present in a majority of cases. In certain epidemics the streptococcus took first place. In all his studies, taken together, he isolated the pneumococcus in 50 per cent of cases and the streptococcus in 23 per cent. He calls attention to his finding of the enterococcus in 29 per cent of cases. He insists that the staphylococcus is not a cause of bronchopneumonia.

Knowing that immunity to streptococcus is difficult to develop and that it is relatively easy to produce an immunity to the pneumococcus and enterococcus, Dufourt prepared a vaccine that contained (per cubic centimeter): pneumococcus I, II and III, 400 million; enterococcus, 400 million, and staphylococcus, 200 million. The staphylococci were added to guard against cutaneous and mucosal infections, frequently found in nurslings with bronchopneumonia. This vaccine is known throughout France as the Weill-Dufourt vaccine.

The author then quotes statistics showing a mortality rate of 65 per cent in 26 untreated patients and a rate of 31 per cent in 26 patients treated with his vaccine. In 200 cases reported to the Lausanne Congress the rate was 27 per cent in the treated patients and 55 per cent in those not treated. In the years 1921, 1922 and 1923, without vaccine, the mortality rate was 64 per cent, and in the three succeeding years in which vaccine therapy was used the rate was 25 per cent. The vaccine is injected subcutaneously, 0.5 cc. the first day and 1 cc. each day thereafter for six, eight or ten days, until the fever drops and the chest signs begin to clear up. No reaction follows the use of the vaccine other than an occasional urticaria or local redness at the site of injection in patients sensitive to proteins.

TURNER, Chicago.

TWO CASES OF EXUDATIVE PERICARDITIS. MARIO LAUREATI, Pediatria **39**:872 (Aug. 15) 1931.

Two cases of exudative pericarditis are reported in which the author was able to follow the clinical signs of progressive mitral involvement. Both cases were secondary to acute rheumatic polyarthritis, and occurred in a girl of 11 years and a boy of 14 years. The author discusses the varieties of this disease, roentgenologic aid in diagnosis, medical treatment and certain proposed surgical procedures.

SIGNORELLI, New Orleans.

MULTIPLE EXOSTOSES, CHONDRODYSPLASIA, CHONDROMATOSIS. G. CAREDDU and V. ROSSI, Riv. di clin. pediat. **29**:377 (May) 1931.

The three types of body alterations, exostoses, chondrodysplasia and chondromatosis, although roentgenologically different, are considered by the authors as being only manifestations of the same fundamental bone condition. This conception is mainly based on a study of nine subjects in the same family who showed one or another of these conditions. The family tree is constructed for four generations (twenty-four individuals). Familial disorders of bone development are discussed. The disease shows different characteristics according to the age of the patient.

HIGGINS, Boston.

VENOUS PRESSURE IN CHILDREN UNDER PHYSIOLOGIC AND PATHOLOGIC CONDITIONS. A. BERNARDI, Riv. di clin. pediat. **29**:589, 1931.

Venous pressure is taken with the body and arms in a horizontal position. A vein at the elbow is punctured with a needle and the pressure measured on a manometer. Venous pressure is lowest in the new-born infant; it doubles at about the sixth year and triples at puberty. The rise is gradual. In chronic or acute respiratory infections, no change from the normal is found unless there is failure of the right side of the heart. In cases of cardiac decompensation, there is a rise in venous pressure; persistence of this rise in spite of therapy is a bad prognostic sign. In cases of diphtheritic paralysis and of toxic and atrophic intestinal disturbances, venous pressure diminishes.

HIGGINS, Boston.

THE PROCESS OF ENDOCARDITIS IN EARLY CHILDHOOD. B. DE VECCHI, Scritti med. dedicati a Carlo Comba, ediz., Riv. di clin. pediat., 1929, p. 599.

In children up to 5 years of age who died of infectious and toxic diseases (diphtheria, bronchopneumonia, meningitis and enteritis), a microscopic examination of the heart valves showed in nearly every case alterations that were certainly inflammatory. They were not always apparent macroscopically since they were not accompanied by the formation of a thrombus. These processes may represent the initial stage of endocarditis and progress to distinct valvular defects.

HIGGINS, Boston.

TWO CASES OF MALIGNANT LYMPHOGRANULOMATOSIS WITH SEROFIBRINOUS PLEURISY. L. MORQUIO, Arch. argent. de pediat. **1**:573 (Dec.) 1930.

The author presents a detailed discussion of the history, pathology, clinical picture and treatment of malignant lymphogranulomatosis or Hodgkin's disease. He describes two cases, in a girl and a boy, 13 and 11 years of age respectively, who presented a typical clinical and pathologic picture of the disease, or what the author calls an adenosplenopleuritic syndrome. Both patients presented, in addition, an extensive serofibrinous pleural effusion. Symptoms of pressure on the mediastinal structures or dyspnea were entirely absent in one of the patients in spite of the fact that the pleural effusion was extensive enough to produce a total displacement of the heart to the right.

The author brings out the fact that the pleural effusion of Hodgkin's disease closely resembles that of tuberculosis in that it is also very extensive and recurs rapidly after paracentesis. In fact, it has been called "pseudotuberculous" by some authors. The tuberculin reaction and the results of guinea-pig inoculation are consistently negative in this form of pleurisy. This effusion fluid is rich in fibrin and leukocytes; among the latter either the polymorphonuclear or the mononuclear forms may predominate, so that it is an exudate rather than a transudate. The effusion is due to the pleural irritation set up by the lymphogranulomatous infiltrations.

A marked melanoderma, i. e., a pigmentation similar to that present in Addison's disease, was a prominent feature in one of the patients. This, according to the author, could be accounted for by the presence of extensive granulomatous infiltration in the suprarenal glands which was revealed at autopsy.

SCHLUTZ, Chicago.

A CASE OF CORRIGAN'S DISEASE IN CHILDHOOD. R. C. AGUIRRE and A. PUGLISI, Arch. argent. de pediat. **2**:103 (March) 1931.

The authors describe a case of Corrigan's disease in a boy, 14 years old, which is interesting because of the rare occurrence of a pure aortic lesion in childhood. The illness began to manifest itself by a precordial pain which began two months before the patient's admission to the clinic. Physical examination revealed all the signs characteristic of the disease: Corrigan's pulse, Duroziez's sign, capillary pulsation, etc. The diagnosis was confirmed by an orthodiagram and electrocardiogram. The etiology in this case remains unknown. Syphilis and rheumatic fever had been ruled out.

SCHLUTZ, Chicago.

A CASE OF HIRSCHSPRUNG'S SYNDROME. M. ARTIGAS, But. Soc. Catalana de pediat. **1**:54 (July) 1928.

The various theories concerning Hirschsprung's syndrome are discussed, and a case is reported in a patient aged 20 months with typical symptoms dating from 11 months of age. The interval between stools was as long as fourteen days. Roentgenograms revealed an enormously dilated colon. Symptoms of obstruction developed and were relieved by breaking up large hard fecaliths by means of forceps per rectum. The patient responded to stimulation of peristalsis together with the use of oil, massage and antirachitic treatment. The infant was pronounced cured in four months.

WATSON, Elmhurst, Ill.

JUSTIFIED DIAGNOSTIC ERROR IN A CASE OF HYDATID PULMONARY CYST. SALVAT ESPASA, But. Soc. Catalana de pediat. **1**:71 (April) 1928.

A pleural inflammatory process about a hydatid lung cyst, as well as the character of the fluid obtained on the first tap, obscured the physical and roentgenologic observations. A second tap revealed the hydatid nature of the lesion.

WATSON, Elmhurst, Ill.

CLINICAL OBSERVATIONS ON NONTUBERCULOUS SPONTANEOUS PNEUMOTHORAX IN INFANCY. S. I. BETTINOTTE and M. T. VALLINO, Rev. de especialid. **6**:36 (June) 1931.

Three cases of nontuberculous spontaneous pneumothorax are presented. The first two were due to lung abscess, and the third to a cortical pleuritis of nontuberculous origin.

SANFORD, Chicago.

THE SO-CALLED THYMIC SYNDROME. SCHWEIZER, O. H. SENET and A. LLAMBIAS, Rev. de especialid. **6**:40 (June) 1931.

A 5 months old child had cyanosis and dyspnea on inspiration, opisthotonos and vomiting. The temperature was 39.5 C. (103.1 F.). On examination, a lobulated tumor was palpated in the jugular fossa. Several roentgen treatments apparently brought improvement. The authors believe it was an adenophlegmon of the suprasternal ganglion.

SANFORD, Chicago.

THE ETIOLOGY OF BRONCHIECTASIS. L. IHM, Arch. f. Kinderh. **92**:170 (Feb. 13) 1931.

Two cases are presented, both in children, 15 years of age, in whom bronchiectasis was present with endocarditis and cardiac insufficiency. In these cases and, the author believes, in many others the etiology is injury to the respiratory tract through secondary infection.

SANFORD, Chicago.

PYURIA CAUSED BY THE COLON BACILLUS. M. FRANK, Arch. f. Kinderh. **92**:254 (Feb. 13) 1931.

The author cultured Bacillus coli in thirty-one cases of pyuria (twenty-six infants and five older children). By the use of various sugar culture mediums to test the biochemistry of the organisms, fifteen different types were found. The type occurring in the largest number was Bacterium neapolitanum, but many cases showed both this and B. coli-commune.

SANFORD, Chicago.

LOBAR PNEUMONIA IN INFANTS AND CHILDREN. P. EIWIN and L. SELDITSCH, Arch. f. Kinderh. **92**:270 (Feb. 13) 1931.

The observations are from the authors' clinic in the State Institute at Kief. Of the group studied, 18.3 per cent were under 3 months of age, 20.7 per cent between 3 and 6 months, 31.4 per cent between 6 and 12 months and 29.6 per cent between 1 and 2 years. Of 280 cases, the right upper lobe was involved in 37, the right lower in 35, the left upper in 6, the left lower in 31 and two lobes in 145. Thirty-one and eight-tenths per cent of the cases occurred in the spring, 18.8 per cent in the summer, 23.8 per cent in the fall and 25.6 per cent in the winter. Sixty-one per cent were boys and 39 per cent girls. Of the children of good nutrition 20 per cent died, of those of medium nutrition 26 per cent died and of those of poor nutrition 52 per cent died.

SANFORD, Chicago.

Nervous Diseases

THE FEEBLE-MINDED PROBLEM. WALTER M. ENGLISH, Am. J. Psychiat. **11**:1 (July) 1931.

Feeblemindedness is increasing alarmingly in all civilized countries. In the United States there are 600,000 people with a mentality below 7 years and 1,200,000 with a mentality of from 7 to 9 years. In every 100 aments, there are 5 idiots, 20 imbeciles and 75 feebleminded persons. The amentia is hereditary in 80 per cent; in 20 per cent it is the result of impairment, not of the germ, but of normal brain growth, the impairment being permanent and incurable.

The solution to the problem lies in inhibiting the procreation of the 80 per cent by legal sterilization. The common belief that the inability to procreate is conducive to greater immorality is challenged by these statistics: Up to January, 1928, 8,515 operations for eugenic sterilization were performed, 4,517 on males and 3,998 on females. Quoting Gosney and Popenoe: "There has not been a single instance discoverable . . . in which a sterilized feebleminded male has

been a sex delinquent." Of the feebleminded females, 9 in 12 had been sexually delinquent prior to sterilization, whereas after the operation was performed and the girls were placed on parole, only 1 in 12 proved delinquent.

JAHR, Omaha.

UNDERWATER GYMNASTICS. C. L. LOWMAN, J. A. M. A. **97**:1074 (Oct. 10) 1931.

There is a misconception that this physical therapy modality is the treatment for paralysis by means of swimming. Muscle reeducation under water is not swimming. The chief danger in the objection is that swimming instructors will get the idea that they are competent to treat patients with paralysis and other conditions in the water, with the result that improper exercises will tend to strengthen the normal muscles and increase the tendency to contractures by their overaction against weakened opponents. The principles of this treatment and the methods of training technicians, together with pool hygiene, are discussed.

BONAR, Salt Lake City.

SIGNIFICANT PROBLEMS IN ACUTE ANTERIOR POLIOMYELITIS. GEORGE DRAPER, J. A. M. A. **97**:1139 (Oct. 17) 1931.

The most pressing needs in the question of acute anterior poliomyelitis are: knowledge of the exact way of transmission, a sure diagnosis in the preparalytic stage and a satisfactory method of protective immunization. The serum of blood from recovered patients will neutralize the virus, but it is necessary to introduce the serum at such a time that it may combine effectively with the virus, and this is before the virus has made its biologic union with the tissues of the central nervous system. The brief interval between the moment of choroid plexus penetration and the moment of virus-cell union is the precious period during which serum may neutralize the invading virus and prevent paralysis. The objection to giving the serum intraspinally at the time of diagnostic puncture is that the choroid barrier, which is ordinarily remarkably resistant, is completely abolished by such a procedure. The choroid barrier may well be the important constitutional factor that protects the patient from paralysis. The author concludes by stating that a preparalytic, in fact, a preataxic tremor stage diagnosis of poliomyelitis can and should be made. The time relationships between the systemic phase, the passage period and the ataxic tremor phase are fairly well indicated by the correlation of clinical signs and spinal fluid observations. Since immune serum can block paralysis in monkeys infected with the virus, and having the diagnostic facts at one's disposal, one should be able to prevent the paralysis in all but the few cases in which the central nervous system phase arrives apparently as the first symptom of the disease.

BONAR, Salt Lake City.

THE KETOGENIC DIET IN THE TREATMENT OF EPILEPSY IN CHILDREN. FLORENCE E. WARNER, New York State J. Med. **31**:1036 (Aug. 15) 1931.

Complete disappearance of seizures is effected in about 33 per cent of the patients put on the ketogenic diet. The diet should be continued for six months after seizures have stopped. Frequent examinations of urine should be made as a check on the maintenance of acidosis. The parents should be trained in making these examinations and should be instructed in the calculation of the diet and the use of food tables.

AIKMAN, Rochester, N. Y.

PHYSICAL THERAPY IN INFANTILE PARALYSIS. RICHARD KOVACS, New York State J. Med. **31**:1078 (Sept. 1) 1931.

During the acute stage of infantile paralysis the paralyzed muscles should be kept at rest and the joints immobilized by plaster casts. Early spinal roentgen therapy may be of advantage, and direct spinal diathermy has given good results.

Thermal radiation from an infra-red generator is preferred by the author. During the convalescent and chronic stages the case should be carefully studied by electrical methods. "The greater majority of muscles are weakened rather than paralyzed." For this reason good results can be obtained by physical therapy even though the case may have been of long standing. Radiation from an infra-red or luminous heat generator or from a hot whirlpool bath is used. Diathermy is also employed. Only light massage is necessary. Active exercise is advised, sometimes with the patient supported by a harness in a heated pool of water. Electrical stimulation must be skilfully used if the best results are to be obtained. Unipolar muscular stimulation is superior to the bipolar method. Electrical treatment need never be painful. "Long persistent treatment is the keynote of success." Frequent electrical testing is advised, and cooperation with the pediatrician and orthopedic surgeons is urged.

AIKMAN, Rochester, N. Y.

THE TREATMENT OF EPILEPSY IN CHILDHOOD. M. G. PETERMAN, Kinderärztl. Praxis **2**:97 (March) 1931.

The author states that epilepsy is a constitutional disease with convulsions as one of the symptoms. The convulsions are due to a disturbance of the water metabolism. The best methods of treatment are a hunger diet, phenobarbital, a decreased water intake and the ketogenic diet. The conclusion seems justified that a disturbed water metabolism is the chief factor in the etiology of true epilepsy.

HUENEKENS, Minneapolis.

ENCEPHALOGRAPHY AND THE INDICATIONS FOR ITS PRACTICAL USE. ALBERT ECKSTEIN, Kinderärztl. Praxis **2**:104 (March) 1931.

Eckstein recommends encephalography in the diagnosis of internal and external hydrocephalus due to various causes, but it is of especial importance in the diagnosis and localization of tumors of the brain.

HUENEKENS, Minneapolis.

CRITICISMS OF THE BINET-SIMON INTELLIGENCE TEST. PAUL VÁRADI, Monatschr. f. Kinderh. **51**:110 (Oct.) 1931.

In the course of school examinations the author tested 124 children from 6 to 10 years of age. He found that the tests were answered very well, and believes that they are really too simple. He thinks that children could easily answer questions assigned to the group a year older.

GERSTLEY, Chicago.

THE RELATIONS BETWEEN BLOOD SUGAR AND SPINAL FLUID SUGAR. ELIZABETH HOENIG, Ztschr. f. Kinderh. **51**:473, 1931.

By the simultaneous testing of sugar in the blood and spinal fluid, a study was made of the quotient $\frac{\text{blood sugar}}{\text{spinal fluid sugar}}$ in fifty patients with nerve diseases. Hoenig's observations were made on patients aged from 5 months to 14 years, who gave a certain constancy in the quotient, on the average from 1.8 to 1.79; indeed this occurred in normal children who showed no signs of meningitis or encephalitis. In patients who had meningitis of various etiology there was considerable variation in the quotient, and even an increase up to 46.5, which was caused by the diminution of the spinal fluid sugar. There was a great increase in the blood sugar, which was caused mostly by convulsions, but in part by direct action on the sugar center. In none of them was there a hyperglycorrhachia. Two patients with acute encephalitis and three patients in a postencephalitic state showed sugar values in the blood and spinal fluid that were within normal limits; occasionally they were relatively low. When the fluctuation in the sugar content of the spinal fluid is being considered, the sugar content of the blood must be remembered, since with an increase of the latter, and no corresponding increase

of the spinal fluid sugar, it must be assumed that there is a disturbance in the passage of sugar from blood to spinal fluid, even if normal values for sugar in the spinal fluid are found. It is noteworthy that usually in serous meningitis there is a normal quotient, as there is in nerve disturbances and convulsions in other infectious diseases of childhood.

EMERSON, Boston.

ACID-BASE METABOLISM: THE INFLUENCE OF LARGE DOSES OF RACEMIC LACTIC ACID ON INFANTILE TETANY. H. FASOLD, Ztschr. f. Kinderh. **51**:535, 1931.

Large quantities of free lactic acid were fed to a baby with manifest tetany, which was completely burned, but caused an acidosis that could be recognized by the increased output of phosphoric acid and ammonia. The mechanical irritability of the nerves diminished. Lactic acid caused an extraordinary increase in the output of chlorine, which was apparently to be traced to the washing out of an edema.

EMERSON, Boston.

Diseases of the Eye

HEREDITARY JUVENILE GLAUCOMA SIMPLEX. R. H. COURTNEY and EMORY HILL, J. A. M. A. **97**:1602 (Nov. 28) 1931.

There is a type of glaucoma that is hereditary. It occurs usually in the second or third decade of life, is unaccompanied by the usual signs of glaucoma in later life, such as a small cornea, a shallow anterior chamber, ametropia and a large lens, and is unassociated with other congenital defects, such as aniridia and coloboma. The glaucoma factor is a dominant one and follows the same hereditary laws as brown irides. This type of glaucoma, while it should be classified as chronic glaucoma, to distinguish it from the acute congestive type, runs a rather rapid course and necessitates early diagnosis and surgical treatment. Miotics or other hypotensive drugs do not affect its course.

BONAR, Salt Lake City, Utah.

AMAUROSIS DUE TO ETHYLHYDROCUPREINE. REPORT OF A CASE AND CURE. PAULINA STANOWSKY and SAUL I. BETTINOTTI, Arch. de oftal., Buenos Aires **6**:589 (July) 1931.

After reference to the frequent use and mode of employment of ethylhydrocupreine in the treatment for pneumonic purulent pleurisies and occasional ocular lesions that may lead to total amaurosis, the authors report a case in a child 2 years of age; ethylhydrocupreine was employed in injections in relatively small doses, but washing out of the pleural cavity with ethylhydrocupreine was prolonged for a long period, and after sixty days mydriasis, pallor of the optic disk and loss of sight developed. The employment of ethylhydrocupreine was suspended and acetylcholine chloride and strychnine sulphate were given internally as a retinal vasodilator and nerve stimulant. Pilocarpine was instilled locally. After two months of treatment, the pupillary reaction and sight had been recovered and the retinal vessels had returned to their normal caliber.

The ocular symptoms dependent on quinine or ethylhydrocupreine intoxication can be classified under two heads: (1) those occurring without any appreciable ophthalmoscopic lesion, and (2) those occurring with lesions, in the form of (*a*) contraction of the retinal vessels and pallor of the optic disk and retina, and (*b*) narrowing of the arteries, tortuosity and dilatation of the veins and papillary edema with occasional hemorrhages. The subjective symptoms consist of sudden blindness with symptoms of retinal ischemia.

The modus operandi by which blindness is brought about has given rise to much discussion; it seems to be of a similar nature to that occurring after severe loss of blood, i. e., by means of a retinal ischemia from vascular spasm, which

manifests itself by retinal and papillary pallor and contraction of the arteries. This is deemed sufficient, by some authors (Uhthoff and Aberdoff) for the production of lesions of the ganglion cells and axis cylinder degeneration, while others (Velhagen and Foster) believe that some toxic action on these tissue elements is necessary, as in their cases and experiments changes were observed early in the microscopic structure of the tissues, which is not explainable solely by the vascular theory.

As regards treatment, the authors consider the essential indications to be: suppression of the use of the drug, with the employment of vasodilators and nerve stimulants. Rollet recommends the use of atropine as a vasodilator. In the reported case the authors did not utilize it, owing to the susceptibility of the child to the drug, preferring instillations of pilocarpine with a view to favoring endo-ocular circulation, and injections of acetylcholine chloride to stimulate the peripheral circulation. Simultaneously they used strychnine.

The authors conclude that ethylhydrocupreine can be employed only in moderate doses with careful and constant watching of the vision, pupillary reaction and ocular fundus and with immediate suspension of the drug at the first sign of a toxic action followed by immediate use of vasodilatatory drugs.

FINLAY, Havana, Cuba. [ARCH. OPHTH.]

FRÖHLICH'S SYNDROME WITH POLYDACTYLISM, RETINITIS PIGMENTOSA AND MENTAL INFERIORITY. JORGE ORGAZ, Rev. méd. latino-am. **16**:966 (April) 1931.

A boy, aged 14 years, presented congenital obesity, hypoplasia of the genitals, six fingers on one hand, six toes on each foot, retinitis pigmentosa and mental deficiency. Hereditary syphilis and consanguinity of the parents were possible etiologic factors.

DWYER, Kansas City, Mo.

THE DEVELOPMENT OF CONGENITAL CORNEAL OPACITIES. RUDOLPH HOFFMANN, Arch. f. Augenh. **105**:162, 1931.

Two main causes have been considered for the development of congenital opacities in the cornea: (1) inflammatory processes during fetal life and (2) developmental anomalies. The majority of recent opinions have been in favor of developmental defects. Peters and others consider anomalies of the lens to be the primary factor, whereas Seefelder holds the view that the primary cause is a defect in the endothelium of the cornea. A case that supports Peters' point of view is presented: A 5 year old girl had corneal opacities in both eyes since birth. One brother had congenital defects consisting of opacities in the lens capsules and marked pupillary membranes. The other children and the mother had normal eyes. In the patient under consideration, the right cornea was clear save for one spot where there was a dense opacity against which the lens was plastered. The latter was clear with the exception of its point of contact with the cornea. The corneal endothelium was present throughout the cornea except at the point where the lens was fastened. There was an incomplete atypical coloboma of the iris. No changes could be seen in the vitreous or in the fundus. The left eye was similar to the right with the addition of a partial dislocation of the lens. The author concludes that the corneal opacities must certainly have been due to a congenital developmental anomaly, since there were no signs of any previous inflammation and since there were other evidences of developmental anomalies present, i. e., coloboma of the iris. He considers it probable that there was a defect in the cutting off of the lens from the ectoderm, and that hence the endothelium never developed in this spot.

ADLER, Philadelphia. [ARCH. OPHTH.]

IRIDOCYCLITIS GONORRHOEICA IN INFANCY. HERMANN BRENTANO, Monatschr. f. Kinderh. **50**:317, 1931.

The author reports an unusual case of gonorrheal iridocyclitis, giving the clinical picture of a pseudoglioma. The disease developed in a 4 months old baby, associated with a general gonorrheal polyarthritis. In the absence of any demonstrable source the author believes that the infection was congenital; this possibility can be questioned, however, as a congenital gonorrheal infection is exceedingly rare.

GERSTLEY, Chicago.

ACUTE IDIOPATHIC MENINGEAL HEMORRHAGE. H. SECKEL, Monatschr. f. Kinderh. **50**:386, 1931.

The author reports two cases of idiopathic meningeal hemorrhage occurring in girls aged 10 and 12½ years, respectively. The disease might be confused with pachymeningitis hemorrhagica interna, except that in idiopathic hemorrhage the onset is very sudden with an apoplectiform seizure, the clinical picture is like meningitis from the immediate onset, and the spinal fluid is always macroscopically bloody and usually low in xanthochrome, cells and albumin. Then too, idiopathic hemorrhage does not occur in infancy. Points common to the two diseases are somnolence, headache, vomiting, fever, bradycardia, rigid neck, Kernig's sign and disturbances of reflex. In the two cases reported the patients recovered.

GERSTLEY, Chicago.

AMAUROTIC IDIOCY OF THE JUVENILE TYPE. ERICH HASSLER and W. SCHOLZ, Monatschr. f. Kinderh. **50**:400, 1931.

Amaurotic idiocy has been divided into four groups: 1. The infantile or Tay-Sachs type, with the characteristic cherry red spot in the macula lutea, affects Jewish children almost exclusively and develops within the first two years. 2. In 1905, a juvenile form was described simultaneously by Vogt and Spielmeyer, with much the same symptomatology except that it occurs in non-Jewish children, does not show the characteristic eye changes, develops at the age of 6 years and runs a more chronic course. 3. Later, Bielschowsky described a late infantile form, beginning in the third or fourth year, but without the cherry red spot. 4. Recently, Kufs described a late form occurring in puberty. Little has been written about the late infantile and juvenile form, largely owing to difficulty in diagnosis. The authors report a case in a 7 year old child in whom the diagnosis of amaurotic idiocy was made. To confirm the diagnosis and with the permission of the parents, a tiny piece of the brain substance was removed from the frontal lobe. Microscopic examination confirmed the diagnosis. Three pathologic plates are shown.

GERSTLEY, Chicago.

TREATMENT FOR CHOREA WITH PHENYLETHYLHYDANTOIN. CARL STAMM, Monatschr. f. Kinderh. **50**:409, 1931.

The author reports excellent results in three cases of chorea using phenylethylhydantoin in doses of 0.1 Gm. three times daily for from eight to twelve days. No fever or exanthem developed. The disease healed rapidly and there were no recurrences. Unquestionably fever and an exanthem diminish the symptoms of chorea. Possibly phenylethylhydantoin, as it frequently produces fever and an exanthem, benefits chorea by producing changes in the body metabolism.

GERSTLEY, Chicago.

Diseases of the Ear, Nose and Throat

OTITIS MEDIA AS A PEDIATRICIAN SEES IT. JOSEPH BRENNEMANN, J. A. M. A. **97**:449 (Aug. 15) 1931.

The author points out that the pediatrician of necessity is well informed about otitis media because he is the one who sees the patient for the underlying throat infection before the ear is involved. He therefore acquires extensive and practical knowledge of the developmental period of middle ear disease and is able to prognosticate with some assurance in the early case. Pain persisting in spite of the use of 5 per cent phenol in glycerin means a progressive condition leading usually to spontaneous rupture or paracentesis. Redness of the drum and swelling along the handle of the malleus do not call for paracentesis. Blebs on the drum are evidence of external otitis and do not indicate a severe otitis media, rather the reverse. Surgical intervention is indicated with persistent bulging of the drum above and about the handle of the malleus. Drums that rupture spontaneously and drain freely fare as well as those which are incised. The author is not in sympathy with the conception that the drum should always be incised in otitis media. Irrigation is contraindicated except for an occasional clearcut indication. Wiping with a dry cotton swab that touches the drum is advocated.

BONAR, Salt Lake City.

THE EFFECT OF TONSILLECTOMY IN ALLERGIC CONDITIONS. STEARNS S. BULLEN, J. Allergy **2**:310 (July) 1931.

From the study of 600 patients of various ages and the records of 2,000 school children presented by Dr. Albert D. Kaiser, the conclusions are reached that (1) "tonsillectomy does not aid in improving the results of treatment of nasal or pulmonary manifestations of allergy; rare exceptions may occur; (2) nasal or pulmonary manifestations of allergy are as liable to occur in an individual whose tonsils have been removed as in one who retains his tonsils."

HOYER, Cincinnati.

BATHING AND AURAL DISEASE. JOHN E. G. MCGIBBON, Brit. M. J. **2**:343 (Aug. 22) 1931.

1. A series of seventeen patients who suffered from acute ear disease attributed to bathing is reported. Of this series, sixteen patients had suffered from a previous aural lesion or some existing abnormality of the adjacent upper respiratory tract.

2. The proportion of bathers in this series who contracted ear disease is relatively greater among the "clean" sea bathers than it is among the "polluted" bath bathers.

3. In view of conclusions 1 and 2, it may be assumed that acute aural disease following bathing is usually an autogenous infection, and occasionally only is it caused by infection derived from the water of public swimming baths.

4. In addition to the measures of personal and public hygiene advocated by Daggett and Cove-Smith, it is advisable, though maybe impracticable, that any person who contemplates bathing should be examined at least once by a doctor in regard to the condition of the ears, nose, etc. The latter measure certainly could be carried out during the routine examination of school children.

5. Any person found to be suffering from aural, nasal or pharyngeal abnormality should be warned of the danger attached to bathing in either the sea or in swimming baths.

ROYSTER, University, Va.

Diseases of the Skin

SCLERODERMA WITH SCLERODACTYLIA: REPORT OF THREE CASES WITH ROENTGEN FINDINGS. LOIS EDEIKEN, Am. J. Roentgenol. **22**:42 (July) 1929.

Three cases of scleroderma with sclerodactylia are reported. All showed bone absorption of the tips of some of the distal phalanges, and one showed increased calcium content in the ends of the phalanges. The other two showed small calcareous concretions in the finger tips. The presence of the latter combined with the absorption of the finger tips appears to be characteristic of sclerodactylia.

STULIK, Chicago.

WOOD'S GLASS IN THE DIAGNOSIS OF RINGWORM. JOHN KINNEAR, Brit. M. J. **1**:791 (May 9) 1931.

Kinnear's experience with Wood's glass is that it is indispensable, but that it has some definite limitations. Hairs infected by Microsporon audouini are fluorescent in light filtered through Wood's glass, with a fluorescence that is a characteristic brilliant green, constant and coextensive with the infection. But hairs infected by other forms of ringworm cannot be detected by this method with any certainty. Hairs affected by favus give a faint fluorescence. Almost any scaly condition of the skin gives a fluorescence because of the fluorescent properties of keratin, but in microsporon ringworm infection the fluorescence is due to the presence of M. audouini. Petrolatum in the scalp gives an intense blue fluorescence, which may hide that due to ringworm. Any ordinary white light may be used for illumination, if it is of sufficient intensity, and ordinary glass does not impede the necessary rays, so that condensers, etc., may be used. The fluorescing properties of the different types of fungus are considered separately.

RATTNER, Chicago [ARCH. DERMAT. & SYPH.].

A CASE OF ERYTHRO-EDEMA. FRANK J. LEES, Brit. M. J. **1**:844 (May 16) 1931.

This is the report of an infant, aged 6 months, who presented the characteristic picture of a pink nose and pink cheeks set in a pale face, watery eyes, photophobia and an aspect of misery. The child was extremely restless and had fever, diarrhea alternating with constipation, and a pseudoparalysis of the cervical muscles and muscles of the legs. She recovered in five months under treatment that was purely symptomatic.

RATTNER, Chicago [ARCH. DERMAT. & SYPH.].

LOCALIZED CONGENITAL DEFECTS OF THE SCALP. DAVID M. GREIG, Edinburgh M. J. **38**:341 (June) 1931.

Congenital lesions of the whole thickness of the scalp, not involving any underlying bone, are comparatively rare and the etiology not certain. One form of lesion either is bullous or has a denuded surface; another type is either membranous or cicatricial. They may not be simple varieties but separate entities.

In the first case described by Greig there were defects in the fetal scalp and head, well shown by a watercolor drawing. There were two bullous areas on the scalp near the obelion, and associated lesions on the back of the neck and head, consisting of a posterior rachischisis (spinal fissure) and an occipital defect. Greig next describes another specimen at the museum which is of the membranous type, in which the lesions comprise two sagittal-shaped congenital membranous areas in the midline of the scalp at the cephalic vertex. This child lived only an hour; the cause of death was not stated, but the period of gestation had been only eight months. Other malformations of common types were present.

Greig compares his two specimens with those previously mentioned in the literature, and speculates as to the etiology. In some instances there are congenital defects of the skin on various portions of the body. The scalp lesions may show

a scantiness of hair, while on the trunk the hair, sebaceous glands and sweat glands are scanty or missing. The cicatricial skin type is sometimes present on the arms or legs at birth. The author believes that the defects arise about the end of the second month in utero. Necrosis could follow histolysis of certain structures of the skin before the stratum corneum has developed. The membranous type on the scalp in the sagittal plane near the anterior or posterior fonticulus is probably of endogenous origin, due to an arrest of development. Cicatrices on other portions of the scalp are probably of amniotic origin. The ulcerative and membranous forms found on the hairy scalp are due to arrested development rather than to amniotic adhesions in fetal life.

NEFF, Kansas City, Mo.

URTICARIA: SOME OBSERVATIONS UPON THE VASCULAR REACTIONS IN THE SKIN. KENNETH E. HARRIS, Quart J. Med. **24**:347 (April) 1931.

The author examined the reactions of the skin in subjects suffering from spontaneous urticaria. The mechanism involved in the production of urticaria is the same as the "triple response," described by Lewis in the reaction of the skin to injury. This triple response consists of (*a*) a local dilatation of the arterioles, capillaries and venules by direct action on the vessels; (*b*) a locally increased permeability of the walls of the minute blood vessels by direct action, leading to local edema of the skin, usually called "whealing," and (*c*) a widespread dilatation of the surrounding arterioles, known as the "flare" and resulting from a local axon reflex. The cause of this response is thought to be due to "H-substance" a histamine-like substance liberated from the skin cells. The author presents interesting diagrams showing the spread of the urticarial wheal. Transference tests yielded results that suggested that in cases of spontaneous urticaria a toxic body circulates in the blood capable of producing the spontaneous whealing.

BRADFORD, Rochester, N. Y.

RESEARCHES ON THE CUTANEOUS REACTIONS CALLED "ECZEMA OF NURSLINGS." H. MONTLAUR and MME. H. MONTLAUR, Ann. de dermat. et syph. **2**:737 (July) 1931.

The authors studied a group of nurslings afflicted with eczematous eruptions of various types—intertrigo, eczematoid, generalized seborrheic eczema, etc. They were able to isolate an enterococcus in most of the patients (principally infants from 1 to 5 months of age), both from the stool and from the cutaneous lesions. They found, however, that they could also demonstrate enterococci in the intestinal contents and on the skins of healthy babies. It would therefore seem that this micro-organism, originating in the intestine and spreading to the skin, is normally innocuous but may under suitable conditions have its virulence exalted and become pathogenic, producing the various pictures seen, which might all be properly grouped under the title of "enterococcid," or an "enterococcic dermitis." It was simply a step further in this line of reasoning to attempt to treat the patients with an anti-enterococcic vaccine. This was done, the intradermal method being utilized, and all local treatment being suspended. The results were encouraging. Cure of the skin condition was often effected, together with an amelioration of concomitant digestive troubles in many. Sometimes there was an initial flare-up or extension of lesions followed by rapid improvement as the treatment was continued. This was interpreted as an allergic phenomenon. The majority of the patients required ten injections, though many needed fewer. Babies suffering from other cutaneous disorders, used as controls, were not benefited by the vaccine.

GANDY, Houston, Texas [ARCH. DERMAT & SYPH.].

TRISYNDROME. MILIAN and L. PÉRIN, Bull. Soc. franç. de dermat. et syph. **38**:852 (June) 1931.

A boy, aged 13, injured his knee, and a bullous impetigo supervened. Several days later a generalized eruption developed. It began with a suspicious herald plaque followed by the appearance of scaling macular and papular, papuloedematous and vesicular lesions. The last-named lesions were most numerous on the hands and fingers, resembling a true dyshidrosis. The general picture presented the features of both pityriasis rosea and parakeratosis psoriasiformis (psoriasiform seborrheic dermatitis). Culture of the vesicles yielded a streptococcus in long chains. The question is raised whether the three elements in this condition, streptococcic impetigo, pityriasis rosea and parakeratosis psoriasiformis, were not all due to the same streptococci.

GANDY, Houston, Texas [ARCH. DERMAT & SYPH.].

RÔLE OF THE ENTEROCOCCUS IN INFANTILE ECZEMA. H. MONTLAUR and MME. MONTLAUR, Nourrisson **19**:161 (May) 1931.

Cultures made from the skin lesions produced gram-positive cocci which were identified as enterococci. The same organism was also recovered from the normal skin of healthy infants. Bacteriologic studies of the stools from infants with eczema showed both enterococci and Bacillus coli, the former predominating. Chemical studies of the stools of breast-fed infants showed an increase in the organic acids. The stools of those fed artificially showed no such increase. Intradermal injections of vaccines prepared from streptococci were tried in thirty-two infants with eczema. Negative reactions were present in thirty. The results of intradermal injections of enterococcal vaccine were sometimes positive but usually negative. After the intradermal injections of enterococci the eczematous lesions were temporarily aggravated, and then showed marked improvement. This observation led to the use of the vaccine in a series of infants with eczema, with excellent results. The skin lesions improved or disappeared, and the digestive disturbances were also benefited.

MCCLELLAND, Cleveland.

ERYTHEMA NODOSUM: II. HEART MURMURS IN ERYTHEMA NODOSUM; THE RELATION OF ERYTHEMA NODOSUM TO ACUTE RHEUMATIC FEVER. P. FORRARA, Riv. di clin. pediat. **29**:89 (Feb.) 1931.

The author has assembled statistics from the literature on the incidence of acute arthritis in erythema nodosum, of erythema nodosum in acute rheumatic fever, of tuberculosis (also phlyctenular keratitis) in erythema nodosum, of tonsillitis in erythema nodosum, and of heart murmurs following erythema nodosum. Of the eighteen cases of erythema nodosum personally observed by the author, seven were initiated by tonsillitis (erythematous in six and follicular in one). In three, marked arthritic pain was present. In one, albuminuria was present. In four, cardiac murmurs appeared in the course of the erythema nodosum and persisted. The murmurs were systolic in time, were heard over the body of the heart and not transmitted, and were musical. The author thinks that the murmurs represent a true but slight cardiac lesion. He concludes that erythema nodosum has only a slight resemblance to acute rheumatic fever. While not of a tuberculous nature it is a disease that has a definite association with tuberculosis.

HIGGINS, Boston.

NONSYPHILITIC CONGENITAL PEMPHIGUS. BRIAN, FOUCALT and MICHEL, Med. de los niños **32**:103 (April) 1931.

A boy, aged 2 months, weighed 3,700 Gm. at birth; the placenta weighed 500 Gm. Birth was normal and the puerperium afebrile. The amniotic fluid was very abundant and golden yellow. Numerous pemphigus lesions were present

at birth. A few scars were also present. Vesicles were found on the commissures of the upper lip and on the arms and legs. A golden yellow exudate escaped from these vesicles. Microscopically, this exudate showed no spirochetes, but cultures revealed colonies of cocci. The Wassermann reactions of the mother and child were negative, and mercurial inunctions produced no effect on the lesions which continued to develop for several weeks, culminating in streptococcic abscesses and otitis media. Congenital pemphigus not due to syphilis is rare.

DWYER, Kansas City, Mo.

REPORT OF THE DRESDEN EPIDEMIC OF MICROSPORIA AND ALOPECIA PARVIMACULATA; THEIR RELATIONSHIP. WERTHER, Arch. f. Dermat. u. Syph. **163**:402 (June) 2) 1931.

During the years 1928, 1929 and 1930, there was an epidemic of microsporia and alopecia parvimaculata involving 400 children from 3 to 14 years of age. The incidence of both conditions rose and fell at the same time. The alopecia was characterized by the presence, mainly in the occipital region, of numerous irregular patches ranging in size from that of a small lentil to that of a penny, not always round but occasionally taking the shape of stripes or crossed stripes, sometimes with fusion of several areas to form a large one. The hairs at the periphery showed succulent roots in contradistinction to the dry atrophic roots of those in alopecia areata. Occasionally some atrophy was present. In most cases hair regrew within the areas affected. Werther considers the alopecia to be due to an involvement of the supporting structures of the hair either by the organisms or their toxins in the nature of a microsporid.

MONASH, New York [ARCH. DERMAT. & SYPH.].

THE QUESTION OF SCLERODERMA. R. FISCHL, Arch. f. Kinderh. **92**:237 (Feb. 13) 1931.

The author shows some excellent photomicrographs of skin sections in scleroderma. He believes that it is more of a general systemic disorder affecting the organism than a condition confined locally to the skin.

SANFORD, Chicago.

THE ETIOLOGY OF ERYTHEMA NODOSUM. O. SAXL, Arch. f. Kinderh. **92**:295 (Feb. 13) 1931.

The author found signs of tuberculosis in seven cases of erythema nodosum. He believes that it is a response to a reaction against tuberculosis.

SANFORD, Chicago.

THE OCCURRENCE OF PERLÈCHE (ANGULUS INFECTIOSUS) IN PUBLIC SCHOOL CHILDREN AND A STUDY OF THE BACTERIAL FLORA. FRIEDRICH SCHWAB, Dermat. Wchnschr. **92**:873 (June 13) 1931.

Among the 17,032 school children of Nürnberg, the author found 129 cases of perlèche, 47 in girls and 82 in boys. Bacteriologic studies revealed diplococci, streptococci and staphylococci in various combinations. Lack of cleanliness is a factor of considerable importance.

TAUSSIG, San Francisco. [ARCH. DERMAT. & SYPH.]

TREATMENT FOR INFANTILE ECZEMA WITH GRENZ RAYS. L. DOXIADES, Ztschr. f. Kinderh. **51**:175 (June) 1931.

Doxiades assumes that the favorable therapeutic action of Grenz rays in chronic recurring eczema in childhood is to be explained on the ground that the excessive

production of histamine-like substance in the skin and, consequently, the cause of the skin irritation are prevented. A better result would be obtained if, along with this treatment, a diet poor in protein could be given.

EMERSON, Boston.

THE PROBLEM OF NEVUS FORMATION. P. N. SHISHKINA-LAVEIN, Sov. Vest. dermat. **9**:368 (April) 1931.

The author describes a case of peculiar multiple pigmented nevi in a child who was under observation for three years. During this time different changes took place in the nevi. Some macular nevi became macerated; some raised ones flattened down. A large macular lesion developed many lanugo hairs, and the skin became folded. Some nevi changed into firm tumors, which disappeared later spontaneously. The histologic examination revealed the following: In the upper layers of the nevus there were cells of very different type: spindle cells, flat, multiangular, dendritic pigmented cells, etc. In the lower layers fibers ran crosswise or formed bundles that resembled nerve fibers. The author also discusses the different theories on the formation of nevus cells and the rôle of the dendritic cells which are supposed not only to form pigment but also to carry the pigment from the epidermis cells to the endothelium cells of the vessels and from there into the blood. According to the author, it is possible that in this way the organism receives radiation energy from without. The author sees in the histologic study of his case the confirmation of the theory of Masson of the nervous origin of the nevus cell.

BLOOM, New York [ARCH. DERMAT. & SYPH.].

ECZEMA SEBORRHOICUM: ECZEMA SEBORRHOICUM AND VITAMIN A. F. C. KUIPERS, Nederl. tijdschr. v. geneesk. **75**:1108 (March 7) 1931; 3439 (June 27) 1931, and 3688 (July 14) 1931.

Starting from the idea that vitamin A has a specific trophic influence on certain epithelia of mucous membranes, the influence of this vitamin on the young skin was studied. With the aid of the reaction of Carr and Price the existence of vitamin A in the vernix caseosa of new-born infants was studied. Of the 136 vernices, 78 gave a positive reaction. In fatty substances in the scales of children with eczema seborrhoicum, vitamin A could sometimes be demonstrated with the reaction of Carr and Price; in some instances this was impossible. The children with a positive reaction showed a tendency toward spontaneous recovery, whereas those without vitamin A showed no such tendency. It appeared, moreover, that the alkali reserve of the blood was correlated with the existence or nonexistence of vitamin A in the fatty substance of the skin. Children with alkalosis had no vitamin A. Scheer has already pointed out the alkalosis of children with eczema and the therapeutic effect of his hydrochloric acid milk. The author recommends a method for inducing the skin to absorb vitamin A. He used the Dutch preparation. In many cases the eczema was cured without further treatment within from seven to ten days. In refractory cases hydrochloric acid was added, and often led to a complete recovery.

An investigation of the vernix caseosa of 200 new-born children showed that 32 per cent of them had no vernix; in 17.5 per cent the vernix gave a negative reaction for vitamin A, in 12.5 per cent a weak positive reaction and in 38 per cent a strong positive reaction. It seemed that the feeding of the mother had little influence on the vitamin content of the child's vernix. The vernix caseosa of a uniovular twin showed a large difference in macroscopic appearance as well as in the amount of vitamin A. The author is of the opinion that the composition of the vernix is determined by the child itself and not by the composition of the mother's blood. Two large types of vernix could be distinguished: homogeneous and cloudy. A distinct relation was found between the amount of fat and vitamin A of the vernix and the microscopic condition (homogeneous or not). The vernix

caseosa, therefore, must be regarded as an important product. A further detailed microscopic investigation of the dried vernix showed that with the exception of the outer layer, the cells of the homogeneous vernix are round or oval and that between the cells there is much fat. The cloudy vernix consists of flat cells showing keratosis for the greater part and lying close to each other; between the cells the amount of fat is small. The aforementioned difference in the structure of the vernix caseosa might point to a difference in the functional condition of the skin. The vernix thus could indicate the degree of keratosis during the later months of pregnancy, and the outer layer of the vernix could represent the condition of the skin at birth. This condition would be of great value in determining whether the child develops eczema seborrhoicum or not. A number of children whose vernix had been studied at birth were therefore investigated after the age of 3 months. It was found that when there had been no vernix at birth, eczema seborrhoicum appeared in only 7 per cent. When the vernix at birth had been cloudy, i. e., contained little fat, a small quantity of vitamin A and cells showing much keratosis, the chance of developing eczema seborrhoicum was also small (12 per cent); when, however, the vernix was homogeneous the eczema seborrhoicum appeared in 42 per cent.

VAN CREVELD, Amsterdam, Holland.

Surgery and Orthopedics

A VERY RARE BLADDER TUMOR (FIBROMYOMA) IN A CHILD. E. W. WHITE, J. Urol. **26**:253 (Aug.) 1931.

Five cases of fibromyoma have been reported, the author's making six. The patient was a girl aged 7 years. The symptoms were frequency and difficulty in starting and stopping. The urine was cloudy and had a foul odor. Its reaction was acid, and the albumin and pus were 2 plus. There were no physical findings. An operation was successful. In this condition the diagnosis is made by cystoscopy, and the treatment is surgical.

SANFORD, Chicago.

FUNNEL CHEST DEFORMITY. JOHN G. KUHNS, New England J. Med. **204**:1077 (May 21) 1931.

Funnel chest deformity (pectus excavatum) is a depression at the lower end of the sternum, causing a marked decrease in the anteroposterior diameter of the chest at the xyphoid. Lang found it in 3.5 per cent of first year school children, in equal numbers in both sexes. It occurs usually in those of slender skeletal build, with associated faulty posture. Roentgen examinations show a lowered position of the diaphragm, with a tendency to abdominal visceroptosis. The congenital type may be due to faulty development of the sternum, or possibly to unusual intra-uterine pressure; the acquired form to rickets, causing a disturbance in breathing mechanics. The pathologic investigations of Bein and Frühwald showed that marked displacement of the mediastinal contents, faulty development of the lungs and cardiac hypertrophy may occur, thus inducing fatigue, subnormal health and disease. Treatment should be directed, first, to the avoidance of excessive fatigue, with at least twelve hours' sleep, and rest periods at noon and after school; second, to corrective exercises so that the forward droop of the head and shoulders, the rounded dorsal spina and the prominent abdomen, give way to habitual good carriage; third, to breathing exercises to increase the lateral rib expansion and widen the costal angle. Most writers agree with Steindler that operations are not successful.

GENGENBACH, Denver.

SAFETY PIN IN THE DUODENUM: CASE REPORT. LAWRENCE W. LONG, South. M. J. **24**:866 (Oct.) 1931.

The lodgment of a foreign body in the duodenum is rare. The case reported by the author concerns an infant 27 months old. A few days after the accident

the pin was located in the first portion of the duodenum. On account of its permanent lodgment in this portion of the bowel and the pronounced complaint of pain, an operation was performed and the pin removed. Recovery was uneventful.

SCHLUTZ, Chicago.

THE TIME FACTOR DURING WHICH VASCULAR RESPONSES PERSIST FOLLOWING PERI-ARTERIAL SYMPATHECTOMY. LAMBERT ROGERS, Brit. J. Surg. **19**:52 (July) 1931.

The author found the effects of periarterial sympathectomy to be of a transient nature. They consisted of increased warmth and scaling. In cases of ulceration on the leg there were reparative changes due to an increase in local circulation. This effect usually lasted five weeks. In extirpation of the sympathetic supply to the limb by ramisectomy or ganglionectomy there was a more lasting increase in local circulation.

SUMMERFELDT, Toronto, Canada.

TRAUMATIC ARREST OF EPIPHYSIAL GROWTH AT THE LOWER END OF THE TIBIA. BRYAN MCFARLAND, Brit. J. Surg. **19**:78 (July) 1931.

It has been noted that while only a small proportion of the injuries of the lower end of the radius during epiphyseal growth are followed by a progressive deformity, the reverse happens in the case of injury to the tibia. After trivial trauma at the ankle a deformity giving rise to serious disability may arise. This difference is due to the fact that on injury of the wrist the fall usually displaces the epiphysis and growing cartilage completely, with a slice off the diaphysis. On the other hand, at the ankle the astragalus is firmly held by the tibial and fibular malleoli. Lateral movement is not free, and in children when an inward twist of the foot occurs the astragalus is forcibly adducted, and the inner edge of the upper surface impinges on the inner half of the epiphyseal plate of the tibia and applies a crushing force at this point. At the same time the internal malleolus is forced upward and inward, and the epiphysis breaks at the base of the malleolus. At the time, the disability is transient and slight, but after a year the deformity may be noticed and seen to increase gradually, the ankle "going out" and the shoes wearing away unevenly. Treatment consists in removing a wedge of the fibula and three fourths of the thickness of the tibia just above the ankle joint. Operation should not be done before the patient is 14 years of age, and it is best to wait until he is from 18 to 20 years old.

SUMMERFELDT, Toronto, Canada.

THE OPERATIVE TREATMENT OF POTT'S PARAPLEGIA. G. R. GIRDLESTONE, Brit. J. Surg. **19**:121 (July) 1931.

The author advocates early decompression for Pott's paraplegia. Either a laminectomy or a costotransversectomy is recommended, but it must be stabilized by bone-grafting of the diseased part of the spine. This increases the stability of the spine. Paraplegia rarely occurs in children, because they are kept at rest sufficiently long. In the past ten years twelve patients have been treated. There were two deaths; in the other cases, partial or complete recovery occurred.

SUMMERFELDT, Toronto, Canada.

HIRSCHSPRUNG'S DISEASE. WALTER MERCER, Tr. Med.-Chir. Soc. Edinburgh, 1930-1931, p. 105, in Edinburgh M. J., July, 1931.

The author reports a case of Hirschsprung's disease in which lumbar ganglionectomy and ramisectomy were performed. He states that one need not apologize for reporting an instance of this manifestation. It is quite rare, there having been 5 cases in ten years in the surgical wards of the Edinburgh Royal Infirmary, and

only 3 of these showed a typical idiopathic dilatation, such as occurs in children. In the London Hospital for ten years (from 1900 to 1909) there were 4 cases among 131,000 admissions. The type that occurs in adults past 50 years of age, described by Treves and characterized by the involvement of the pelvic colon alone, is, in fact, a chronic form of volvulus. Mercer repeats some of the interesting facts about true Hirschsprung's disease: it is congenital, but in some cases symptoms are absent for a while at the beginning; the males affected greatly outnumber the females; the pathologic condition is usually in the colon alone; in 33 per cent of the cases it is confined to the sigmoid, where the changes are mild, but later, due to block and extension of the hypertrophy and dilatation to the proximal portion it finally reaches close to the transverse and ascending colon; there is never any evidence of mechanical obstruction or true constriction at the end of the enlarged segment. The author describes the clinical features, the etiology and the treatment. The various operations and what may be expected from them are discussed, the great majority of cases now being cured by cutting off the sympathetic nerve supply to the lower bowel.

Mercer's case was in a 9 year old boy who was constipated even while he was breast fed; he came under observation at 5 years of age, and was operated on four years later. Exploration showed that the dilatation reached its maximum at the middle of the sigmoid, but involved also the left portion of the transverse colon and the upper part of the rectum. Peristaltic waves could be induced by the slightest manipulation. The sympathetic ganglions were easily exposed; the second, third and fourth lumbar as well as the trunk and the ramus were removed well above the second and below the fourth lumbar. The postoperative course was without incident. The photographs of the boy before operation and five months afterward show the remarkable decrease in the size of the abdomen. The patient now gives evidence of being in every way an active, happy boy, whose physical and mental state has been entirely changed.

NEFF, Kansas City, Mo.

TERATOMA OF OVARY. BRAXTON HICKS, Proc. Roy. Soc. Med. **24**:1184 (July) 1931.

A case of teratoma of the ovary was reported in an Italian infant aged 13 months. She was admitted to the hospital in March, 1931, with the complaint that for the last three months the abdomen had been rapidly increasing in size. It was distended with dilatation of the superficial veins, and a large mass was palpable occupying the whole of the right side of the abdomen and extending into the pelvis and to the left of the midline. The patient developed bronchopneumonia and died on April 1. At postmortem examination a large cyst weighing 2 pounds and 12 ounces (1,247.4 Gm.) and apparently arising from the left ovary was found.

WILLIAMSON, New Orleans.

HABITUAL DISLOCATION OF THE PATELLA IN AN INFANT. CARLE ROEDERER, Rev. d'orthop. **17**:647 (Nov.) 1930.

Roederer reports a case of habitual dislocation of the patella in a child 3 years of age. Associated with this condition were a bilateral genu valgum and rickets.

An attempt has been made to improve the genu valgum by the use of external splints and orthopedic appliances, but these measures are only temporary and should be used only until surgical correction of the deformity can be undertaken. Correction of the genu valgum will correct the tendency to dislocation of the patella.

RYAN, Vancouver, B. C.

OBSTETRIC PARALYSIS OF THE ARM: POSTERIOR GLENOID ABUTMENT IN HABITUAL SUBACROMIAL DISLOCATION; SOME CLINICAL SIGNS AT THE ONSET. H. L. ROCHER, Rev. d'orthop. **18**:45 (Jan.) 1931.

In operative treatment of habitual subacromial dislocation in obstetric paralysis of the arm, Rocher builds up a bony block to reenforce the posterior part of the glenoid cavity, using a piece of rib, since that transplant is already slightly curved and best serves the purpose.

In the presence of an obstetric paralytic lesion, within ten days of delivery, a definite loss of color can be noticed in the injured hand and in the lower third of the forearm. Rocher considers this due to vasoconstriction. This loss of color persists for three or four days. If the hand is squeezed to produce further exsanguination, and the blood allowed to return, the resulting color is paler than on the healthy side. He terms this "gauntlet ischemia" and considers sympathetic irritation in its etiology.

A slipping of the superior head of the humerus may simulate a dislocation of the shoulder. In one case the displaced head lay in the axilla. Another important sign is a laxity of the shoulder articulation. This is probably produced by hypotonicity of the muscles and dystrophy of the capsular ligaments. Slowness of response to electrical stimulation is important in prognosis. If the reaction does not improve by the end of the second or third month, a definite lesion will persist.

Early treatment of the internal rotation of the arm is stressed. When the lesions and deformities are established, operative treatment to correct the deformities may prevent further contractures and, by permitting more normal muscular function, decrease the trophic changes already present.

RYAN, Vancouver, B.C.

FEMORAL HERNIA IN A CHILD. L. VELASCO BLANCO and E. M. ESCHEGAREZ, Arch. am. de pediat. **7**:3 (Jan.) 1931.

The authors report a case of femoral hernia in a boy 11 years of age successfully treated by operation. The hernia was the size of a large nut, was easily reducible, with an enlarged femoral ring, and produced no symptoms. There was a history of a fall with injury to the abdomen at the age of 4; since then a tumor mass had been noticed by the mother.

The case is of interest because of the extreme infrequency of femoral hernias in children. According to various statistics they constitute about 0.4 per cent of the total number of hernias in children. The authors are of the opinion that femoral hernias may be acquired or congenital. In the former there exists an outward propulsion of the peritoneum and in the latter a preformed peritoneal diverticulum. A definite sac, closely adherent to the femoral vein, was present in the case reported.

SCHLUTZ, Chicago.

Miscellaneous

ETIOLOGY OF THE ILL-HEALTH OF CHILDREN BORN AFTER MATERNAL PELVIC IRRADIATION: I. UNHEALTHY CHILDREN BORN AFTER PRECONCEPTION PELVIC IRRADIATION. DOUGLAS P. MURPHY and LEOPOLD GOLDSTEIN, Am. J. Roentgenol. **22**:207 (Sept.) 1929.

Twenty-four per cent of 650 pregnancies associated with radium therapy or roentgen irradiation of the pelvis before or after conception ended in abortion; 13 per cent terminated in the birth of unhealthy children, including an anencephalic stillborn infant, a microcephalic infant, a hydrocephalic mongolian idiot and infants with malformed head, heart defects, tracheal defect, etc. One of every 10 or 11 children born after preconception pelvic irradiation was unhealthy, whereas 1 of every 2 born after postconception pelvic irradiation was unhealthy. The ill health of 22 of the 46 unhealthy children born after preconception irradiation was

attributed to prior maternal ill health (6 cases), complications incident to delivery or prematurity (13 cases) and accidental causes (3 cases); 2 unhealthy children later became healthy. The etiology of the ill health of 22 children, including 7 who were seriously defective, could not be determined. Only 1 out of every 59 born after preconception irradiation exhibited some gross anatomic defect of unknown origin, and it is the belief of the author that if the irradiation was the etiologic factor, the defects would have occurred with greater frequency, regularity and uniformity. It cannot be stated with certainty that preconception maternal pelvic irradiation is entirely free from danger to subsequent offspring, because of the occurrence of a few defective children born after such treatment. A bibliography is appended.

STULIK, Chicago.

STRYCHNINE AGAIN RESPONSIBLE FOR LARGE PERCENTAGE OF FATAL POISONINGS OF CHILDREN. Health News (New York State Dept. Health) **7**:195 (Dec. 8) 1930.

Of twenty-three fatal cases of poisoning in children 5 years of age and under in New York State, exclusive of New York City, twelve, or over one-half, were due to the accidental ingestion of strychnine. The figures for 1926, 1927 and 1928 were practically the same.

AIKMAN, Rochester, N. Y.

PHYSICAL MEASUREMENTS AND PHYSIOLOGIC PROCESSES IN YOUNG CHILDREN. W. P. LUCAS and H. B. PRYOR, J. A. M. A. **97**:1127 (Oct. 17) 1931.

In this study an attempt was made to simplify classification of body build by merely comparing width to length of body, a single diameter of the pelvis being chosen for width. The standard deviations indicate that weight varies from the height-weight table twice as much as the width-length index varies from the average at each age when both are measured in per cent. A small beginning has been made in the study of body build as related to allergic conditions. Asthma occurs largely in children of linear type. Of fifty allergic children, those with complaints of asthma and bronchitis had an average width-length index of 152. Those with complaints of eczema and asthma had an index of 165, and those with complaints of eczema and hives, an index of 178.

BONAR, Salt Lake City.

PERIODIC PHYSICAL EXAMINATIONS AND PROPHYLACTIC HEALTH CENTERS. G. SCHREIBER, Rev. internat. de l'enf. **11**:576 (June) 1931.

The value of periodic examinations, beginning in earliest infancy and continuing through life, has been impressed strongly throughout France, particularly since the social insurance system was inaugurated. It is recognized everywhere that the cost of thorough examinations would be more than compensated by the reduced requirements for hospitals and homes for the incurable. Medical inspection of school children, as practiced in the United States and in Belgium, is urged for the pupils of all French schools, and the extension of this provision to applicants for marriage licenses is suggested. It is believed that centers for preventive medicine, established in all of the larger towns and cities with a staff of experts, would be more successful than isolated groups of independent workers, and such a plan is outlined by the author.

AMESSE, Denver.

INFANT MORTALITY IN CUBA. A. A. ABALLI, Bol. Soc. cubana de pediat. **8**:35 (Feb.) 1931.

The author tells of the high infant mortality in Cuba and brings out the necessity for organizing a campaign for the protection of the infant as well as the pregnant and nursing mother.

The following statistics, which are far from being complete, are presented. In Havana for the year 1925 the death rate of children equaled 16 per cent, not including deaths from tuberculosis. For 7,220 children born in 1925 there were 1,196 deaths reported, of which 818 were from gastro-intestinal tract diseases, 175 from respiratory diseases, 171 from congenital debility (not including tuberculosis), 37 from meningitis and 15 from syphilis.

There are no reliable figures for deaths from tuberculosis which, according to the author, are also very numerous. The mortality is higher among the colored race. The predisposing factors for the very high mortality from gastro-intestinal diseases are: the continuous heat and humidity and the great percentage of artificially fed infants because of poor social conditions, the great percentage of illegitimate babies and the lack of facilities for the working mother to nurse her baby. The organizations existing in Cuba at present to aid the mother and infant are few and not well organized. There are very few hospital facilities for children. The first hospital for children in Havana is going to be inaugurated shortly.

The author proposes a new plan for the protection of infancy, to include prenatal and postnatal care of the mother, which consists in having all the organizations for this purpose under one central office which would supervise the work and give the best possible advice to the organizations. The author presents a diagrammatic scheme as to how the various organizations could be interrelated.

SCHLUTZ, Chicago.

PUBLIC AND PRIVATE SOCIAL SERVICE ACTIVITIES FOR CHILDREN IN FRANCE. G. ICHOK, Gesundhfürs. f. d. Kindesalt. **6**:198 (June) 1931.

This article is a summary of social service activities in France.

REICHLE, Cleveland.

A ROENTGEN TABLE FOR BABIES. W. HEILIG, Ztschr. f. Kinderh. **51**:263, 1931.

A table for holding babies comfortably during examination or treatment by x-rays is described.

EMERSON, Boston.

HEMOGLOBIN IN NURSING MOTHERS IN JAPAN. K. ASAI, J. Pediat. (Tokyo), Aug. 20, 1931, no. 375, p. 1160.

The author determined the hemoglobin values (Sahli) in 141 healthy nursing mothers, the ages of the nurslings varying from 1 to 18 months. The results showed the average value to be 67.8 per cent, which is slightly lower than that for the average adult female in Japan (from 70 to 90 per cent). There was no appreciable difference between the primipara and the multipara. There was a tendency for the value to be higher in direct proportion to age. The value seems to be at its highest in the seventh month of parturition, and thereafter it gradually decreases.

KATO, Chicago.

THE BACTERIOLOGY OF THE NIPPLE OF NURSING MOTHERS. H. SUGINO and K. TAKAHASHI, J. Pediat. (Tokyo), Aug. 20, 1931, no. 375, p. 1117.

The authors examined bacteriologically the nipples of ninety-four apparently healthy nursing mothers during a period between two and eighteen months after parturition. They obtained an abundant growth of micro-organisms from a piece of moist but sterile gauze that was used to wipe off the nipple, implants being made on three types of medium. Staphylococcus albus was the predominating organism, others being bacilli of various morphology. Occasionally, the streptococci, diplococci and sarcinae were found. The blood and 4 per cent glycerin agar plates were most satisfactory for the purpose.

KATO, Chicago.

Society Transactions

NEW YORK ACADEMY OF MEDICINE, SECTION OF PEDIATRICS

May 14, 1931

HUGH CHAPLIN, M.D., *Presiding*

A METHOD FOR THE CONTINUOUS INFUSION OF INFANTS. DR. JOHN M. BRUSH.

This article will be published in full in a later issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN.

TREATMENT OF TOXICOSIS WITH THE AID OF A CONTINUOUS INTRAVENOUS DRIP OF DEXTROSE SOLUTION. DR. SAMUEL KARELITZ, with an introduction by DR. BÉLA SCHICK.

This article was published in full in the October, 1931, issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN, page 781.

SUPRARENAL-INSUFFICIENCY AS THE CAUSE OF ACUTE INTESTINAL INTOXICATION AND THE TREATMENT WITH A SUPRARENAL CORTEX EXTRACT. DR. AUBREY B. MACLEAN, RUTH C. SULLIVAN and R. L. ZWEMER.

Many theories have been advanced as to the cause of acute intestinal intoxication. One of the first was probably the climate, as the disease was called summer diarrhea. This was followed by a period during which cow's milk was thought to be the etiologic factor, as the disease occurred more frequently in bottle-fed infants. Improper feeding, with diets too high in fat, sugar or protein, were considered at various times to be at fault. Poor hygienic care has also been suggested as a cause, as infants in institutions and in poor districts appeared to be more susceptible. The presence of infections, as otitis media or mastoiditis, was thought significant. The production of a toxic substance and the abnormal absorption of catabolites have been hypothecated. Failure of excretion of the kidneys has also been described as the essential lesion. The fact that a great number of infants are exposed to one or several of these causes, with the development of intoxication in only a few cases, would suggest that the foregoing conditions play a secondary rôle.

Suprarenal insufficiency as an etiologic factor seems adequately to explain the picture of intestinal intoxication.

In a previous paper, the similarity of the changes in the chemical composition of the blood in these two conditions was pointed out.

Clinically, there is marked similarity. In both, gastro-intestinal upset with diarrhea and vomiting is an early symptom. Loss of appetite is nearly always present, but occasionally in animals, as well as in infants, the appetite remains good as the general condition becomes worse. Dehydration, as shown by dry mucous membranes and loss of tissue turgor, is always present. This is the most characteristic symptom. The mental state is usually dull, but is at times irritable and excited. Decreased peripheral circulation with cold extremities is always present. In the experimental animal there is a subnormal temperature before death. In infants with intoxication, while this is often the case, infections may cause an increase in temperature. Loss of weight is very rapid as death approaches.

Convulsions are a terminal condition in 50 per cent of the experimental adult cats. They occur rarely in adrenalectomized kittens or suprarenalectomized infants with intoxication.

In the urine of both the adrenalectomized cats and the suprarenalectomized infants with intoxication, casts are present.

The pathologic findings in intoxication are usually negative except for some degeneration of the kidneys. Ulcers of the intestine are occasionally found. In experimental suprarenal insufficiency are found cloudy swelling of the kidneys and ulcers of the intestine.

Acute intestinal intoxication occurs only in infants. The age incidence was studied in 200 cases of intoxication; only 1 infant was over 12 months of age. The majority of the babies were between 2 and 6 months of age. It is also true that the morphology of the suprarenal gland in infancy is different from that of the adult. The difference is chiefly in the cortex. The zona granulosa is much less distinct. The three subdivisions are not well marked. The glands assume adult form from 3 years of age to puberty. Moreover, the thymus gland and lymphatic tissues are hyperplastic in the infant in comparison with those of the adult.

The metabolism of the infant seems more delicately adjusted than that of the adult. Gastro-intestinal upsets are more common. They range in severity from cases of mild indigestion to those of acute intestinal intoxication. This, it is felt, is due to a suprarenal function inadequate to the demands put on it in abnormal circumstances. With a mild depression of function may be associated the picture of acute indigestion. With a more severe suppression of function, then, would follow the picture of acute intestinal intoxication.

The suprarenals seem necessary for normal water metabolism. Removal of the glands results in a loss of both salt and water with a picture of dehydration and acidosis. Treatments with fluid alleviate these symptoms and prolong the life of the animal. This effect, however, is only temporary, and death ensues. Some factor supplied by the suprarenal cortex appears necessary for proper water metabolism.

Similarly, infants with acute intestinal intoxication are benefited by the administration of fluids. Only 15 of the 200 infants studied died within twenty-four hours of admission. The greatest number of deaths occurred in the following two weeks. Following the administration of fluid there is a temporary disappearance of the toxic symptoms. The value of fluids is beyond question. Some pediatricians hold that one solution is of much more value than another. There is enough evidence to show that any of the different solutions used will prolong life and, in some cases, effect a cure.

When the nature of the acidosis was under discussion, insulin, epinephrine and bicarbonate of soda were given to see the effect on the carbon dioxide capacity of the plasma. There was no change in the carbon dioxide capacity of the plasma following the administration of insulin. It was noted, however, that convulsions followed very small doses of insulin.

Epinephrine also failed to raise the carbon dioxide capacity of the plasma.

Intravenous bicarbonate of soda caused a temporary elevation of the carbon dioxide capacity. At the same time there was a temporary improvement in the dehydration. It was disappointing to find that the mortality in the 76 cases in which the patients were so treated was 61 per cent, as contrasted with a mortality of 60.5 per cent in the entire series of 200 cases.

Blood, saline and dextrose solutions were also used. They were given intravenously, intraperitoneally and subcutaneously. Dextrose and saline were also administered by continuous infusion. All of these have at times aroused a temporary enthusiasm, but are, of course, only symptomatic treatment.

Before the administration of suprarenal cortex extract to infants with acute intestinal intoxication, the effect on the carbon dioxide capacity of the plasma of normal cats and rabbits was determined. The extract was considered potent if the carbon dioxide capacity was elevated at least 7 per cent by volume over a

period of forty-eight hours. In these normal animals there was also a rise in blood sugar. The nonprotein nitrogen and chlorides remained within normal limits.

The effect of cortical extract on the chemical composition of the blood of adrenalectomized cats was also determined. The variations from normal have been pointed out in a preceding paper. Following the administration of the extract, the carbon dioxide capacity, chlorides, sugar and nonprotein nitrogen returned to normal limits. There was also chemical improvement. The prostrated animal was able to get up and walk about. The appetite also returned, and the animal took both fluid and solid food.

Thirteen patients with acute intestinal intoxication were treated with suprarenal cortex extract. Ten of the thirteen had severe cases. With the exception of two patients, all had received the usual therapy without improvement before administration of the extract. Eight patients were cured and five died. Of the five that died, one showed an abscess of the lung, one had a congenital cerebral defect and another had pulmonary tuberculosis with calcification of the suprarenals. The fourth case showed no pathologic changes. In the fifth case autopsy was refused.

The chemistry showed a fairly typical course. The carbon dioxide capacity of the plasma was elevated in twenty-four hours; it reached normal in forty-eight hours and was at a very high normal in ninety-six hours. The chlorides, as a rule, returned to within normal limits in twenty-four hours. The dextrose showed a rapid increase and gradually returned to a low normal. The nonprotein nitrogen of the blood also returned to normal limits.

In two cases signs of tetany with carpopedal spasms and Chvostek's sign developed. The first patient had a serum calcium of 6 mg. per hundred cubic centimeters with a carbon dioxide capacity of the plasma of 52 per cent by volume. The second patient received a large amount of calcium before a sample of blood was taken for analysis. No other untoward effects were observed.

The improvement in the general physical condition was striking. The appetite was markedly better during the first twelve hours. The dehydration was definitely less in twenty-four hours. The weight curve showed a rapid increase in from three days to one week. There was also improvement of the condition of the stools.

The more detailed figures and graphs used in this paper will be published later.

(From the Chemical Laboratory of the Babies Hospital and the Department of Diseases of Children and the Department of Anatomy, College of Physicians and Surgeons, Columbia University.)

A Comparison of the Chemical Composition of the Blood in Acute Intestinal Intoxication and Experimental Adrenal Insufficiency in Animals. Ruth C. Sullivan, Dr. Aubrey B. MacLean and R. L. Zwemer.

The chemical picture of both acute intestinal intoxication in infants and of adrenal insufficiency in animals is that of a disturbance of salt and water metabolism and of carbohydrate metabolism.

The diarrhea and vomiting characteristic of both bring about a loss of electrolytes and fluid from the body. In the chemical composition of the blood this loss is usually reflected as an acidosis. In experimental adrenal insufficiency there was a marked decrease in the carbon dioxide capacity of the plasma. A similar change was observed in the blood of infants with intestinal intoxication. The carbon dioxide capacity of the plasma has been determined in a series of 122 such infants on admission to the hospital before treatment. Ninety-five per cent showed values less than normal (from 48 to 60 per cent by volume); four figures were in the normal range, and two were above normal, 69 and 92.4 per cent by volume, respectively.

As the change in the chemical composition of the blood depends on the loss of variable amounts of base and acid in the stool and vomitus, some variation is to be expected in individual cases, depending on the relative degree of diarrhea and

vomiting present. If the quantity of base lost exceeds that of acid lost, acidosis occurs. This seems to be the typical picture. In a few cases, however, the loss of acid exceeds the loss of base. Here one may expect either a normal carbon dioxide capacity of the plasma or an increased carbon dioxide capacity, an alkalosis.

Significant changes occur in the chemical composition of the blood of adrenalectomized animals only during the last three days of life. For this reason the chemical composition of the blood in acute intestinal intoxication during the seventy-two hours preceding death has been compared with that in experimental adrenal insufficiency.

Most of the infants had received the usual treatment: parenteral introduction of saline, dextrose and blood, and in some cases bicarbonate of soda. Fluids were forced by mouth. In spite of this therapy an acidosis was present. Eighty-five of the ninety-three cases studied showed a decrease in the carbon dioxide combining power of the plasma. There was, however, some tendency for the carbon dioxide capacity to be greater in these cases than in those without treatment. Fourteen cases showed values within or above the normal range.

The loss of salt and water also causes a shift in the level of the blood chlorides. Where there is marked loss of both chloride and base, there is a decrease in both carbon dioxide capacity of the plasma and chlorides. This was found in adrenalectomized animals.

Of the infants with intoxication on admission to the hospital, before the introduction of either salt or fluid, 14 per cent showed blood chlorides below normal; 41 per cent were within, and 45 per cent were above, the normal range (from 450 to 500 mg. per hundred cubic centimeters of whole blood).

The shift in level of the blood chlorides shows better, perhaps, than the carbon dioxide capacity, the individual differences in the relative amount of acid and base lost. Where the amount of base lost is greater than that of vomitus, the blood chlorides are increased, while the carbon dioxide capacity is decreased. This is the chloride acidosis described by Hamilton. With a greater loss of chlorides and base, the blood chloride is found to be in the normal range. With a still greater depletion of salt, both base and chloride, the blood chlorides drop below the normal limit.

In analyzing the changes obtained in the blood chlorides in intestinal intoxication within seventy-two hours of death, a definite tendency toward a decrease was evident, in spite of the fact that most of the patients had been treated with parenteral saline. In this series 32 per cent showed values less than normal, in contrast with 14 per cent in the untreated series. It is of some significance that with one exception the blood chlorides below the normal range occurred only in the cases in which the patients died.

In both experimental adrenal insufficiency and acute intestinal intoxication of infants there is a disturbance of carbohydrate metabolism. In doubly adrenalectomized animals there was a decrease in the level of the blood sugar. Of the infants with intestinal intoxication on admission to the hospital, before treatment, 65 per cent showed an increase in blood sugar. During the course of the disease they were treated both orally and parenterally with dextrose solution. Nevertheless, on examination of the blood sugar within seventy-two hours of death, the figures were seen to be considerably lower than on admission to the hospital, and in some cases (40 per cent) were even below the lower limit of normal (from 70 to 110 mg. per hundred cubic centimeters).

The oliguria consequent on the dehydration causes a retention of nitrogen. In experimental adrenal insufficiency there was an increase in the nonprotein nitrogen of the blood. In babies with intoxication varying degrees of retention of nitrogen were present. In 80 per cent of the cases studied before treatment, there was some increase in the nonprotein nitrogen of the blood, with only 8 per cent having marked retention, i. e., with the nonprotein nitrogen greater than 70 mg. per hundred cubic centimeters of blood. In the series examined within seventy-two hours of death, nonprotein nitrogen of the blood above the normal range (from 25 to 35 mg. per hundred cubic centimeters) was found in 72 per cent of the cases.

There is again evidence of renal retention in the elevation of the phosphorus of the blood. This was not as consistent a finding as the increase in the nonprotein nitrogen of the blood. Some of the doubly adrenalectomized animals showed figures within the normal range. Others showed a marked increase in phosphorus. The same was true of infants with intestinal intoxication. Fifty-one per cent of the cases studied showed less phosphorus than normal. Twenty-one per cent gave figures in the normal range (from 5 to 6 mg. per hundred cubic centimeters). Twenty-eight per cent showed an increase of phosphorus in the blood.

In the series studied within seventy-two hours of death, most of the figures for phosphorus (82 per cent) lay below the normal level.

A complicating factor here is the question of rickets and the initial level of the phosphorus of the blood.

That phosphorus of the blood plays an essential part in carbohydrate metabolism must also be considered in interpretation of the values for phosphorus obtained. Undoubtedly a disturbance of phosphorus metabolism is associated with the derangement of carbohydrate metabolism found in these two conditions.

It is difficult to compare changes in the chemical composition of the blood in experimental adrenal insufficiency and intestinal intoxication for several reasons.

The clinical course is different. The average duration of life of a cat after removal of the second adrenal gland is ten days. For the first three or four days the animal appears normal. During the next three or four days it refuses solid food and takes only fluids. For two or three days before death it refuses all food. It is at this time that significant chemical changes occur in the blood. In babies, intestinal intoxication is of variable duration. In some infants it lasts only a few days, in others it may extend over a period of several weeks.

In the experimental animal there is an uncomplicated picture of adrenal insufficiency. In the infant the clinical picture is often complicated by an infection —bronchopneumonia, thrush, otitis media, etc.

Moreover, the chemical picture is of necessity distorted in infants by the administration of salt and fluid, a factor that does not have to be considered in the experimental animal.

Nevertheless, in some (individual) cases, the changes in the chemical composition of the blood in intestinal intoxication have been similar in each respect to the changes found in experimental adrenal insufficiency. (From the Chemical Laboratory of the Babies Hospital and the Department of Diseases of Children and of Anatomy, College of Physicians and Surgeons, Columbia University.)

CHICAGO PEDIATRIC SOCIETY

Regular Monthly Meeting, Dec. 15, 1931

HENRY E. IRISH, M.D., *President, Presiding*

DRIED LACTIC ACID MILKS AS A LONG-CONTINUED DIET FOR INFANTS. DR. JULIUS H. HESS, DR. I. MCKY. CHAMBERLAIN and DR. LOUIS S. ROBINS.

A controversy as to the relative value of dried lactic acid milks, liquid lactic acid milks and sweet milk mixtures as a diet for infants over long periods led us to undertake the following study.

As controls, infants were fed breast milk, breast milk complemented with various lactic acid milks, and feedings consisting entirely of cultured fluid lactic acid milk and sweet milk plus lactic acid, U. S. P.

The experiment was started on Dec. 10, 1929, and was carried on for a period of ten months, ending Oct. 10, 1930. Of 186 infants who, with a few exceptions,

were from the new-born service of the obstetric department of the Illinois Research and Educational Hospital, 116 were selected for intensive study. At the end of the experiment, 85 of these infants had been under continual close observation with satisfactory cooperation on the mother's part for a minimum period of four months and a maximum period of ten months.

Eighteen infants were entirely breast fed; nineteen were given breast milk complemented with dried lactic acid milks, fresh cow's milk plus lactic acid, U. S. P., and fresh cultured lactic acid milk; five were fed cultured lactic acid milk exclusively; thirty-four were fed dried lactic acid milk exclusively, and four were fed various combinations of the aforementioned substances.

Supervision of these infants was as complete as possible, great care being taken in the selection of the cases. A full time trained nurse made visits to the homes, and was constantly available to the mothers by telephone.

Feedings were standardized to approximate a food value of 2 ounces (56 Gm.) of cow's milk per pound of body weight in twenty-four hours. Cane sugar was added in amounts of 0.1 ounce (2.8 Gm.) per pound of body weight, and sufficient water to bring the total daily intake of fluid to from 2½ to 3 ounces (70 to 85 Gm.) per pound of body weight was added. Breast-fed infants were allowed to take all the food they desired in a nursing period of twenty minutes.

The administration of cod liver oil was started at 3 weeks, 10 drops being given twice daily; this dosage was increased until 8 cc. was given daily at 3 months. Orange juice was given at 3 weeks, one-half teaspoonful being given twice daily; this was increased until at 3 months 1½ ounces (42.5 Gm.) was given. Cereal was given at 5 months, vegetable soup at 7 months, and banana was added at 9 months. These foods were fed in the same amount to all of the infants.

Sixty-two of the infants took the feedings of lactic acid well, and three infants required the addition of saccharine for a short interval.

Gains in weight for the groups of infants fed the various lactic acid milks were approximately the same, and these gains compared favorably with the accepted normal average gains for the artificially fed infants.

Vomiting was an unusual symptom throughout the period of our study. Colic occurred in a few instances; these cases were mild. Five infants on the feedings of dried lactic acid milk and two on cultured lactic acid milk showed considerable constipation.

During the last two weeks of August and the first week of September, while diarrhea was prevalent in the city, diarrhea developed in ten patients. Three received breast feedings complemented with dried lactic acid milk; four were fed entirely on dried lactic acid milk; two were fed cow's milk, plus lactic acid milk, U. S. P., and one was given cultured sweet milk. All of the patients recovered. The sugar and additional feedings were omitted, but the lactic acid milks were continued in full amounts throughout the illness. The only drug used was camphorated tincture of opium, U. S. P.

Estimations of hemoglobin (Newcomer) were made at monthly intervals throughout the study. There were no outstanding differences in the values for hemoglobin in the various groups studied. The percentage of infections was approximately the same. The various groups of artificially fed infants had more severe infections than the breast-fed ones. We were unable to distinguish definite differences in the convalescence from infections in the infants fed on dried lactic acid milk as compared with those on a diet of sweet milk plus lactic acid, U. S. P.

There was no discernible difference in the time of eruption or quality of the teeth in any of the groups of artificially fed infants.

A number of the infants showed evidence of an eruption of the skin of an eczematoid type. Four of the cases were moderately severe, two developed in infants that were breast fed exclusively, one in an infant fed breast milk complemented with dried lactic acid milk and one in an infant given feedings entirely of dried lactic acid milk. Tests for sensitization of the skin were negative. All of the mild cases cleared spontaneously without change in diet.

Roentgenograms of the long bones were taken in all cases in which clinical rickets was suspected. Only one patient showed marked changes of the bones.

This infant was one of those having moderately severe eczema, and had had severe diarrhea lasting for four weeks. This infant received breast feedings complemented with dried lactic acid milk.

In twelve other cases a diagnosis of clinical rickets was made; one of the infants was entirely breast fed; three received breast feedings complemented with dried lactic acid milk; one, fresh milk plus lactic acid milk, U. S. P.; one, cultured lactic acid milk, and six dried lactic acid milk only. In these twelve cases evidence of mild rickets was shown in the roentgenograms of an infant fed breast milk complemented with dried lactic acid milk, of one fed cow's milk plus lactic acid milk, U. S. P., of one fed cultured lactic acid milk and of one fed dried lactic acid milk.

Dried lactic acid milk can be used satisfactorily as a long-continued food for infants.

DISCUSSION

DR. CRAIG BUTLER: I am much interested to hear of this work, for when it has been necessary to feed a baby on a milk diet high in protein, it has been my habit to maintain that feeding for what is commonly considered an unsafe length of time. I usually use albumin milk, and often keep the child on that diet until it is from 8 to 10 months of age, when the vegetable and cereal feedings are well established. Often in the second or third month the albumin milk is mixed into the cereal and vegetable water, and it has been my experience that infants thus fed have developed as well or better than infants given the usual feedings. I have obtained no unfavorable results from continuing this food for a considerable time. It is interesting to hear a carefully evaluated check-up on the results of similar feedings.

INFECTIOUS DIARRHEA IN CHILDREN, WITH BACTERIOLOGIC OBSERVATIONS. DR. MAURICE L. BLATT and DR. NOEL SHAW.

In the summer of 1930 there was an increased incidence of diarrhea in children entering the pediatric wards of Cook County Hospital. Many of these patients were admitted with intense toxemia; some were in coma. The stools were soft or watery, as frequent as thirty a day in severe cases and small in amount, and almost uniformly contained blood and mucus.

The temperature was not high in the moderately ill patients, but it reached 105 or 106 F. in the severe cases. The temperature fell within from twenty-four to forty-eight hours in most of the cases in which recovery occurred. This improvement occurred in response to nursing, care and dietary treatment. The pulse and respiratory rates remained high for several days thereafter. In the majority of the cases convalescence was completed within ten days after the patient's entrance into the hospital. When death did not occur within forty-eight hours, the prognosis was good.

The syndrome continued during the summer of 1931, reaching its peak in August. The first cases in both years were seen in June and the last in November. The disease seemed to be similar to the ulcerative type of diarrhea seen in Chicago prior to 1915.

To determine the causative agent of this serious disease, cultures of the stools were made, stools being collected in sterile diapers or sterile bed pans.

Experience proved that the organisms responsible for the local lesion in the bowels were best found in the mucus. A small portion of mucus was plated out on 2 per cent lactose litmus plates. When the suspected organisms were obtained in pure culture, they were identified by cultured and serologic methods. Two per cent solutions of sugar in plain broth were used for fermentation tests. The organism usually isolated from the diarrheal patients in 1930 and in 1931 appeared to be the same, but showed changes in ability to ferment sugars. Twenty-two strains isolated in 1930 fermented dextrose and mannite readily and maltose and sucrose in from two to ten days. Late fermentation of lactose did not occur, except in the two Sonne cases. Fifty-five strains were isolated in 1931 from cultures of specimens from sixty-five patients. Twenty-three strains have been identified; three

were of the paratyphoid, two of the Sonne and two of the Shiga group. The remaining 16, or about 70 per cent, of the apparent dysentery forms were the same as those isolated the previous year. Although this type of organism does not conform strictly to the classification of Bergy, it is considered to be of the Flexner type. This conforms to the British classification. Agglutination tests with stock Flexner serum gave positive results, usually through 1 : 1,280.

DISCUSSION

DR. MAURICE L. BLATT: We recognize that it is a rather serious matter to present a mass of bacteriologic work before a clinical group, and yet the work is of such unusual interest that this seems desirable. Recently Dr. Yu reported his work on the transmutation of the diphtheria organism from one group to another by means of culture mediums to which antiserum was added. In the dysentery group a similar transmutation in the gastro-intestinal tract of children seems possible. The classification by Dr. Shaw of the organisms isolated in different persons makes one think of such a possibility. It is our hope that by the continuation of this work we may be able to develop a method of producing a serum of high titer usable during the summer season.

DR. CLIFFORD G. GRULEE: Few of us realize the amount of work that has been done in the bacteriologic report represented by this paper. Few have the patience for it, and it is interesting and rejuvenating. In the early days of my practice one of the interesting events was the discovery by Strong and Flexner of their types of dysentery bacilli, and in the literature up to 1903 one finds many papers of this sort. One fact that stands out is that this report concerns older children, while Strong and Flexner's concerned babies. In Chicago we thought that there was a good deal of useless discussion about the Flexner bacillus, which they were finding in the East, in New York and Boston, because we could not find it here, try as we would. Soon afterward, the type of diarrhea changed entirely, and, as Dr. Shaw said, the former type is now reappearing. Something can be said about the kind of weather we have had. We must remember that we have had a very hot and extended summer. In the earlier reports much was said about hot weather.

Since the infants were not affected to the same degree, we may be sure that the food of infants is better controlled than is that of older children, and it is possible that the causes which Dr. Shaw outlined in the paper may be factors in this new outbreak of dysentery, which is probably of the Flexner type, or what we used to speak of as the Flexner type.

DR. NOEL SHAW: This type of dysentery is moderately contagious, and the factors of contagion seem much the same as those in typhoid. It was common to have a group of children from one family enter the hospital. We need a potent serum including the causative organisms usually found in cases of dysentery of this region. It may be helpful in the extremely toxic cases which otherwise prove fatal.

PHILADELPHIA PEDIATRIC SOCIETY

Stated Meeting, Jan. 12, 1932

JOHN P. SCOTT, M.D., *President, in the Chair*

THE TREATMENT OF POSTURAL DEFORMITIES IN CHILDREN. Presented by DR. DEFOREST P. WILLARD.

Postural defects occur most frequently either at the beginning of the assumption of the erect position or at the adolescent age. In the lower extremities, owing to the inefficient action of muscles, pronation (incorrect alinement of the feet with the normal weight-bearing line) and knock-knee occur. Correction by raising the

inner border of the heel and adding a resilient pad under the instep, associated with stimulation of the muscles by baking, massage and exercise, is often necessary.

In the spine, exaggeration of the normal anteroposterior curves and the lateral curvature (scoliosis) are both due to deficiency of the muscles. Subjective symptoms usually occur after prolonged abnormality, causing distortion of the thoracic and abdominal cavities, which affects the organs contained within them. Weakness of the muscles is treated by heat, massage and voluntary training; braces or corsets should be used only in conjunction with muscular exercises.

Lateral curvatures occur most commonly between the tenth and fifteenth years. These are: postural, which appears as a single curve due to unilateral skeletal defects in addition to lack of muscle tone, and structural, which appears as a double or triple curvature due to compensatory changes after a long-standing postural curve. In the latter, the deviation is fixed and cannot be entirely corrected by manipulation. The vertebral bodies are deformed and rotated, and the ribs displaced. Curvatures of the postural group are treated by removal of etiologic factors, by application of braces and by gymnastics to strengthen the muscles. In the structural cases, treatment usually must be carried further. The application of forcible pressure by properly applied plaster casts or of lateral traction with the patient in the recumbent position to attain correction, and of braces or operative fusion of the spine to prevent increase in deformity is necessary.

The care of these patients is a responsibility that the orthopedic surgeon must assume, but the diagnosis in the vast majority of cases must be made by the family physician and pediatrician, and the responsibility of recognizing these cases in the early or postural stage, when treatment offers a good chance of finished cure, depends absolutely on him.

SPASTIC PARALYSIS OF CHILDHOOD. Presented by DR. A. BRUCE GILL.

Cerebral spastic palsies of childhood are due to prenatal causes, such as lack of normal development of the brain, syphilis, cerebral softening or sclerosis; to injuries received at the time of birth, and to certain diseases, such as meningitis, encephalitis, whooping cough and exanthemas during the first few years of life. Of these groups, the first causes the greatest physical disability and mental impairment, the second group comes next in importance, and the third group last.

The symptomatology varies with the degree of injury or the lack of development of the brain. Mental impairment is found in many children; hypertonicity of muscles with rigidity, various typical deformities of both the upper and lower extremities, athetosis, incoordination of muscular movements and exaggeration of reflexes vary according to the nature of the lesion.

The prognosis depends principally on the degree of mental enfeeblement and on the extent and severity of muscular incoordination.

The cases of the second group, which are due to hemorrhage, usually meningeal and occasionally cerebral, occur during difficult and prolonged labor, or are caused by asphyxia of the child at birth. Lumbar puncture should be done to determine the presence of blood in the cerebrospinal fluid and to note the pressure. Repeated punctures should be made in case of increased pressure. The operation of cerebral decompression may even be considered in severe cases. Care on the part of the obstetrician on delivery of the child might prevent a certain percentage of cerebral birth palsies.

If the mental defect is severe, treatment is of no avail. Muscular training is essential in all cases that are amenable to treatment, both operative and nonoperative. Operative treatment for relief of deformities is practical. The lengthening of tendons is necessary in cases of structural shortening. Operations that have been used to lessen spasticity are the Foerster, the Stoffel, the Royal and methods of crushing motor nerves or injecting alcohol into them. Transplantations of muscles are occasionally of advantage. Operations that have stood the test of time are muscular transplantation in selected cases, lengthening of tendons and the Stoffel operation.

Many patients with spastic paralysis can be greatly improved by operation and by long-continued and faithful perseverance in muscular training.

Book Reviews

Die Fehlerziehung in der Pathologie des Kindes. By Dr. Josef K. Friedjung. Price, 4.80 marks. Pp. 100. Berlin: Julius Springer, 1931.

The author of this book is a practicing pediatrician in Vienna and a follower of freudian teachings. As the title of the book suggests, the subject is handled from a practical point of view. No particular theories are emphasized and enlarged on; the author manages to keep his balance fairly well in spite of his freudian leanings.

He first gives a historical review of the subject and of the development of new ideas in the field of child psychology. It is to be regretted that in this chapter, as in the rest of the book, he completely ignores any contribution outside of the German literature. He apparently is ignorant of the tremendous development that has taken place in this field in the United States. After a sketchy description of the emotional and instinct life of the child, he gives an outline of the most important points in training the child. In the chapter on the relationship between the pediatrician and the child, he gives some useful practical suggestions about handling difficult children during examination and treatment. The short chapter on the character of problem children is rather incomplete. The clinical description of problem children is strongly under the influence of the psychoanalytic theories. His classification of problems of environment is quite interesting. He writes about love-tired, love-hungry children and about children who are the objects of disagreement between parents, and he discusses problems in the relationship between brothers and sisters.

In his explanation of the origin of psychoneurosis in the child, Friedjung accepts the Oedipus complex as the basis of this problem. From the pediatric point of view, the chapter on the influence of behavior problems on the course of different diseases is particularly interesting. In this chapter he emphasizes that personality and body constitution will decidedly influence the reactions that any disease process produces in the patient.

In the chapter on prevention and treatment of psychoneuroses in children, the author emphasizes the importance of parental education. In the treatment a change of environment seems to be the most important factor, according to Friedjung, and he admits that psychoanalysis is practically never successful in children.

On the whole, this short book will be helpful to general practitioners and pediatricians who are interested in the psychic problems of childhood. Its greatest value is that it is written by a practical man for practitioners.

Röntgendiagnostik und Strahlentherapie in der Kinderheilkunde. By Dr. Joseph Becker. Cloth. Price, 48 marks. Pp. 302, with 293 illustrations. Berlin: Julius Springer, 1931.

This book takes up a short history of Roentgen's discovery of the x-rays and a brief description of x-ray apparatus, tubes, etc. Then in well organized chapters the author describes normal and pathologic conditions met with in children. There are many excellent roentgen illustrations showing practically all pathologic conditions met with in the field of pediatrics. The specific technic for making roentgen exposures is given.

Of special interest is the chapter on hypothyroidism, with examples of cases studied over a period of years. The work on encephalography is described in detail, and the illustrations are instructive.

The chapter on roentgen therapy describes the treatment used in various foreign clinics. Many of the paragraphs on specific diseases give the technic used in treatment, but omit the results to be expected; others are written in detail and are excellent.

The rôle of the x-rays in children is well covered; the book will prove valuable to the pediatrician as a reference book to the x-rays.

Les affections de l'oreille. By Max Meyer. Price, 40 francs. Pp. 201, with 25 figures and 6 plates. Paris: Gauthier-Villars & Cie, 1932.

This book is a translation by Dr. P. Gauthier-Villars of the German work on the subject. It contains chapters on instruments, physiology of the ear, acute and chronic conditions, traumatic diseases and the deaf and dumb child. It is devoted exclusively to diseases of the ear in children. It is quite readable and interesting, and the figures are well reproduced.

Praktische Differentialdiagnostik. By Dr. Walter Pflüger and Dr. Joseph Husler. Price, 50 marks. Pp. 151. Dresden: Theodore Steinkopff, 1931.

The subject matter of this small volume is classified according to symptoms rather than according to diseases. Symptoms as they appear in new-born infants and in children are discussed in three sections, with the differential characteristics of the diseases causing such symptoms in each of the age periods. Since the work is intended primarily as an aid to the physician in bedside diagnosis, emphasis is placed on the data derived from the history, observation of the child and its environment and physical examination. Laboratory diagnosis is omitted except when it is of essential importance, and then it is not discussed in detail.

Special attention is given to the variation in symptoms in different children due to differences in underlying constitution. The exudative and neuropathic diatheses in particular are described as responsible for many atypical reactions. The importance of viewing the child as a whole rather than concentrating on isolated organs is emphasized throughout, and the interpretation of symptoms from this point of view is probably the chief contribution of the book.

Directory of Pediatric Societies

INTERNATIONAL

International Association of Preventive Pediatrics

President: Professor Taillens, Lausanne, Switzerland.
Secretary: Dr. P. Oltramare, rue Decandolle, Geneva, Switzerland.
Place: Geneva, Switzerland. Time: July 15, 1932.

International Pediatric Congress

President: Dr. George Frederic Still, 28 Queen Anne St., London, W. 1.
Place: London. Time: 1933.

FOREIGN

Royal Society of Medicine, Section for the Study of Disease in Children

President: Sir Henry Gauvain, 125 Harley St., W. 1, London.
Secretary: Dr. E. I. Lloyd, 33 Wimpole St., W. 1, London.

NATIONAL

American Medical Association, Scientific Assembly, Section on Diseases of Children

Chairman: Dr. Jay I. Durand, 1305, 4th Ave., Seattle.
Secretary: Dr. Alfred A. Walker, Highland Plaza Apartments, Birmingham, Ala.
Place: New Orleans. Time: May 9-13, 1932.

American Academy of Pediatrics

President: Dr. John L. Morse, 319 Longwood Ave., Boston.
Secretary: Dr. C. G. Grulee, 636 Church St., Evanston, Ill.
Place: New Orleans. Time: May 13-14, 1932.

American Child Health Association

President: Dr. Samuel McC. Hamill, 1822 Spruce St., Philadelphia.
Secretary: Dr. Philip Van Ingen, 125 E. 71st St., New York.

American Hospital Association, Section on Children's Hospitals

President: Dr. Thomas B. Cooley, 7815 E. Jefferson Ave., Detroit.
Secretary: Miss Bena M. Henderson, 721 N. 17th St., Milwaukee.
Place: Detroit. Time: September 12-16, 1932.

American Pediatric Society

President: Dr. Howard Childs Carpenter, 1805 Spruce St., Philadelphia.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid, St. Louis.
Place: Rochester, Minn. Time: May 26-28, 1932.

Association of American Teachers of the Diseases of Children

President: Dr. Ralph M. Tyson, 334 S. 21st St., Philadelphia.
Secretary: Dr. Oscar Reiss, 1930 Wilshire Blvd., Los Angeles.
Place New Orleans. Time: May 9-10, 1932.

Canadian Society for the Study of Diseases of Children

President: Dr. G. A. Campbell, 164 Metcalfe St., Ottawa, Ontario.
Secretary-Treasurer: Dr. L. P. MacHaffie, 162 Clemow Ave., Ottawa, Ontario.

SECTIONAL

Central States Pediatric Society

President: Dr. Frank C. Neff, 406 W. 34th St., Kansas City, Mo.
Secretary: Dr. A. H. Parmelee, 715 Lake St., Oak Park, Ill.
Place: Kansas City, Mo. Time: Fall, 1932.

North Pacific Pediatric Society

President: Dr. A. Howard Spohn, 925 West Georgia St., Vancouver, B. C.
Secretary: Dr. L. Howard Smith, 734 Medical Arts Bldg., Portland, Ore.

Southern Medical Association, Section on Pediatrics

Chairman: Dr. Horton Casparis, Vanderbilt University Hospital, Nashville, Tenn.
Secretary: Dr. Luther W. Holloway, 117 W. Duval St., Jacksonville, Fla.
Place: Birmingham, Ala. Time: November 16-18, 1932.

STATE

Alabama Pediatric Society

President: Dr. Thomas J. McElhenney, 1722, 2nd Ave., Bessemer.
Secretary-Treasurer: Dr. John W. Simpson, 1117 S. 22nd St., Birmingham.

Georgia Pediatric Society

President: Dr. Charles E. Boynton, 118 Forrest Ave., N. E., Atlanta.
Secretary-Treasurer: Dr. Roger W. Dickson, 33 Ponce de Leon Ave., N. E., Atlanta.

Louisiana State Pediatric Society

President: Dr. R. T. Lucas, Shreveport, La.
Secretary-Treasurer: Dr. Suzanne Schaeffer, Chailie Bldg., New Orleans.

Medical Society of State of New York

Chairman: Dr. Albert D. Kaiser, 16 N. Goodman St., Rochester.
Secretary: Dr. Adolph G. G. De Sanctis, 12 E. 11th St., New York.
Place: Buffalo. Time: May, 1932.

Nebraska Pediatric Society

President: Dr. H. B. Hamilton, 434 Aquila Court Bldg., Omaha.
Secretary: Dr. George L. Clark, 1817 Vinton St., Omaha.
Place: As announced by committee. Time: Second Thursday of each month from October to June, inclusive, 6 p. m.

North Carolina Pediatric Society

President: Dr. Yates W. Faison, 121 W. 7th St., Charlotte.
Secretary: Dr. E. K. McLean, 121 W. 7th St., Charlotte.
Place: Various children's hospitals. Time: Twice a year.

Oklahoma State Pediatric Society

President: Dr. C. E. Bradley, Medical Arts Bldg., Tulsa.
Secretary: Dr. G. H. Harrison, 1200 N. Walker St., Oklahoma City.
Place: Tulsa. Time: May 14, 1932.

South Carolina Pediatric Society

President: Dr. T. D. Dotterer, 1512 Marion, Columbia.
Secretary-Treasurer: Dr. Julian P. Price, 117 W. Cheves St., Florence.

Texas Pediatric Society

President: Dr. J. H. Park, Jr., 3717 Main St., Houston.
Secretary-Treasurer: Dr. P. E. Luecke, 4105 Live Oak St., Dallas.

VIRGINIA PEDIATRIC SOCIETY

President: Dr. St. Geo. Grinnan, 925 W. Grace St., Richmond.
Secretary-Treasurer: Dr. J. B. Stone, 2042 Park Ave., Richmond.

LOCAL

ACADEMY OF MEDICINE OF CLEVELAND, PEDIATRIC SECTION

Chairman: Dr. J. E. McClelland, 10515 Carnegie Ave., Cleveland.
Secretary: Dr. P. G. Albrecht, 2009 Adelbert Rd., Cleveland.
Place: 2009 Adelbert Road. Time: Four meetings, from September to May.

ACADEMY OF MEDICINE, TORONTO, SECTION OF PEDIATRICS

Secretary: Dr. Lawrence Murray, 1870 Bloor St., W., Toronto.
President: Dr. Gladys Boyd, 56 DeLisle St., Toronto.

BRONX PEDIATRIC SOCIETY

President: Dr. Joseph Golomb, 496 E. 17th St., New York.
Secretary: Dr. E. Leonard Benjamin, 2229 Valentine Ave., New York.
Place: Concourse Plaza, 161st St. and Grand Concourse. Time: Second Wednesday of each month, except June, July, August and September.

BROOKLYN PEDIATRIC SOCIETY

President: Dr. Irwin Schiff, 658 Eastern Parkway, Brooklyn.
Secretary: Dr. Louis A. Koch, 62 Pierrepont St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Last Wednesday of each month, except June, July and August.

CENTRAL NEW YORK PEDIATRIC CLUB

President: Dr. Frank Vander Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Fourth Thursday of October, January and April.

CHICAGO PEDIATRIC SOCIETY

President: Dr. Henry E. Irish, 432 S. Lincoln St., Chicago.
Secretary: Dr. Bert I. Beverly, 8 S. Michigan Ave., Chicago.
Place: City Club. Time: Third Tuesday of each month.

DALLAS COUNTY PEDIATRIC SOCIETY

President: Dr. Gordon B. McFarland, Medical Arts Bldg., Dallas, Texas.
Secretary: Dr. Harold T. Nesbit, Medical Arts Bldg., Dallas, Texas.
Place: Bradford Memorial Hospital. Time: 1 p. m., first and third Saturdays of each month.

DETROIT PEDIATRIC SOCIETY

President: Dr. Charles Wilson, 10 Peterboro St., Detroit.
Secretary: Dr. Joseph A. Johnston, Henry Ford Hospital, Detroit.
Place: Children's Hospital of Michigan. Time: No fixed date; approximately once a month.

FULTON COUNTY MEDICAL SOCIETY, PEDIATRIC SECTION (ATLANTA, GA.)

Chairman: T. Bolling Gay, 384 Peachtree St., Atlanta.
Secretary: Dr. Roger W. Dickson, 33 Ponce de Leon Ave., N. E., Atlanta.
Place: Academy of Medicine, 32 Howard St. Time: Second Thursday of each month from October to April, 8 p. m.

MEMPHIS PEDIATRIC SOCIETY

President: Dr. William R. Graves, 1193 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. Harry J. Jacobson, 1193 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month.

Milwaukee Pediatric Society

President: Dr. G. H. Fellman, 231 W. Wisconsin Ave., Milwaukee.
Secretary: Dr. George F. Kelly, 161 W. Wisconsin Ave., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

New England Pediatric Society

President: Dr. Lewis Webb Hill, 319 Longwood Ave., Boston.
Secretary: Dr. Gerald Hoeffel, 319 Longwood Ave., Boston.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. Herbert B. Wilcox, 39 E. 75th St., New York.
Secretary: Dr. John Caffey, 50 Haven Ave., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

Northern California Pediatric Society

President: Dr. Edward B. Shaw, 384 Post St., San Francisco.
Secretary-Treasurer: Dr. Lloyd Hardgrave, 384 Post St., San Francisco.
Place: Various teaching schools. Time: Monthly.

Northwestern Pediatric Society

President: Dr. Samuel Amberg, Mayo Clinic, Rochester, Minn.
Secretary: Dr. Alexander Stewart, 459 Lowry Medical Arts Bldg., St. Paul.

Philadelhia Pediatric Society

President: Dr. John P. Scott, 2040 Pine St., Philadelphia.
Secretary: Dr. John D. Donnelly, 115 Bryn Mawr Ave., Bala-Cynwyd, Pa.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to June, inclusive.

Pittsburgh Pediatric Society

President: Dr. David H. Boyd, 200, 9th St., Pittsburgh.
Secretary: Dr. Theodore O. Elterich, 724 Highland Bldg., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate months from October to April, inclusive.

Richmond Pediatric Society

President: Dr. John S. Weitzel, 3103 W. Franklin St., Richmond, Va.
Secretary-Treasurer: Dr. W. E. Chapin, 922 Floyd Ave., Richmond, Va.
Place: Retreat for the Sick, 2621 Grove Ave. Time: First Thursday of each month (other than during the summer).

Rochester Pediatric Society

President: Dr. S. W. Clausen, Strong Memorial Hospital, Rochester, N. Y.
Secretary: Dr. F. W. Bush, 221 S. Goodman St., Rochester, N. Y.
Place: Arranged by program committee. Time: First Friday of each month from October to May.

Rocky Mountain Pediatric Society

President: Dr. C. H. Platz, Fort Collins, Colo.
Secretary: Dr. R. H. Verploeg, 1850 Gilpin St., Denver.
Place: Children's Hospital, Denver. Time: Third Saturday of each month from September to May, inclusive, 2:30 p. m.

St. Louis Pediatric Society

President: Dr. Gustave Lippmann, 3720 Washington Blvd., St. Louis.
Secretary-Treasurer: Dr. Katherine Bain, 3720 Washington Blvd., St. Louis.
Place: St. Louis Medical Society. Time: Third Friday of every month.

Seattle Pediatric Society

President: Dr. C. L. Smith, 1215, 4th Ave., Seattle.
Secretary: Dr. N. W. Murphy, 515 Cobb Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, 7 p. m.

Southwestern Pediatric Society

President: Dr. William M. Happ, 523 W. 6th St., Los Angeles.
Secretary: Dr. Jeanette Harrison, 1136 W. 6th St., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. Henry G. Poncher, 5325 Kenmore Ave., Chicago.
Secretary: Dr. John P. Parsons, 320 S. Division St., Ann Arbor, Mich.
Place: Ann Arbor, Mich. Time: November, 1932.

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